

## WEST Search History

DATE: Tuesday, April 18, 2006

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
	<i>DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ</i>		
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<input type="checkbox"/>	L33	L3 and L21	63
<input type="checkbox"/>	L32	L31 and L26	4
<input type="checkbox"/>	L31	L30 and L24	667
<input type="checkbox"/>	L30	stabil\$	1066686
<input type="checkbox"/>	L29	L19 and L24	20
<input type="checkbox"/>	L28	L26 and L21	4
<input type="checkbox"/>	L27	L26 abd k21	0
<input type="checkbox"/>	L26	L16.ab.	295
<input type="checkbox"/>	L25	s L17.ab.	1
<input type="checkbox"/>	L24	L21 and L16	768
<input type="checkbox"/>	L23	L21 and L19	20
<input type="checkbox"/>	L22	L21 and L20	23
<input type="checkbox"/>	L21	ewing\$ NEAR2 sarcoma	2014
<input type="checkbox"/>	L20	zyxin	181
<input type="checkbox"/>	L19	cofilin	216
<input type="checkbox"/>	L18	L17 and L14	3
<input type="checkbox"/>	L17	actin	26040
<input type="checkbox"/>	L16	actin	26040
<input type="checkbox"/>	L15	L14 and L13	2
<input type="checkbox"/>	L14	(auclair or amsellem or hervy or subra).in.	337
<input type="checkbox"/>	L13	L12 or L11 or L10	22041
<input type="checkbox"/>	L12	(435/7.23)! [CCLS]	3264
<input type="checkbox"/>	L11	(424/93.21)! [CCLS]	1908
<input type="checkbox"/>	L10	(514/12  514/44  514/9)! [CCLS]	17734
<input type="checkbox"/>	L9	L8 AND L3	1
<input type="checkbox"/>	L8	20040191230.pn.	1
<input type="checkbox"/>	L7	L5 not @ay>2001	4
<input type="checkbox"/>	L6	L5 not @py>2001	0
<input type="checkbox"/>	L5	L4 and sarcoma	83
<input type="checkbox"/>	L4	L3 and ewing\$	83

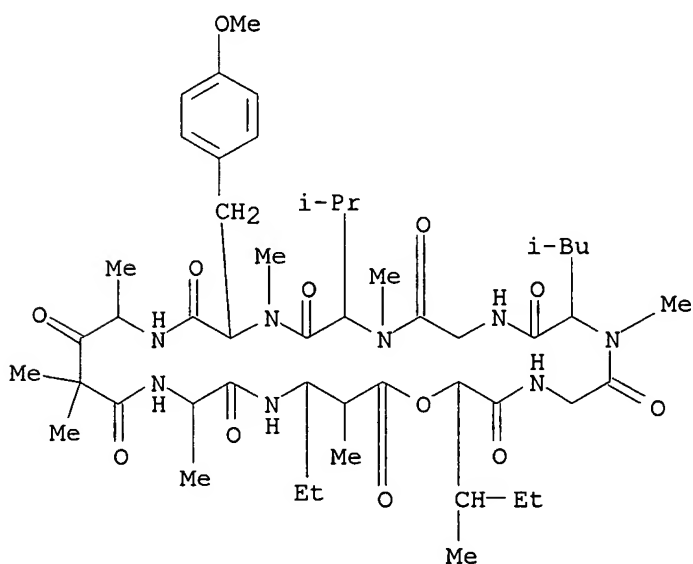
<input type="checkbox"/>	L3	jasplakinolide	201
<input type="checkbox"/>	L2	L1 and ewing\$	1
<input type="checkbox"/>	L1	dolastatin 11	11

END OF SEARCH HISTORY

RN 111517-68-1 REGISTRY  
 CN Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-dimethyl-L-tyrosyl-(4S)-4-amino-2,2-dimethyl-3-oxopentanoyl] (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.  
 CN **Dolastatin 11**  
 OTHER NAMES:  
 CN NSC 606195  
 FS PROTEIN SEQUENCE; STEREOSEARCH  
 SQL 8  
 NTE modified (modifications unspecified)

type	-----	location	-----	description
bridge	Gly-1	-	Oaa-8	covalent bridge
uncommon	Oaa-6	-	-	-
uncommon	Oaa-8	-	-	-

SEQ 1 GLGVYXAX  
 MF C50 H80 N8 O12  
 SR CA  
 LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)  
 DT.CA Caplus document type: Dissertation; Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)  
 RLD.NP Roles for non-specific derivatives from non-patents: PREP (Preparation); PRP (Properties)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

22 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

CCESSION NUMBER: 2005:184733 CAPLUS  
 DOCUMENT NUMBER: 142:371546  
 TITLE: The actin cytoskeleton-associated protein  
**zyxin** acts as a tumor suppressor in  
**Ewing** tumor cells  
 AUTHOR(S): Amsellem, Valerie; Kryszke, Marie-Helene; Hervy,  
 Martial; Subra, Frederic; Athman, Rafika; Leh, Herve;  
 Brachet-Ducos, Corinne; Auclair, Christian  
 CORPORATE SOURCE: CNRS UMR 8113, Laboratoire de Biotechnologie et  
 Pharmacologie genetique appliquee, Ecole Normale  
 Superieure de Cachan, Cachan, 94230, Fr.  
 SOURCE: Experimental Cell Research (2005), 304(2), 443-456  
 CODEN: ECREAL; ISSN: 0014-4827  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:583223 CAPLUS  
 DOCUMENT NUMBER: 141:188806  
 TITLE: Molecular mechanisms of CD99-induced  
 caspase-independent cell death and cell-cell adhesion  
 in **Ewing**'s sarcoma cells: actin and  
**zyxin** as key intracellular mediators  
 AUTHOR(S): Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania;  
 Bernard, Ghislaine; Manara, Maria Cristina; Benini,  
 Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi,  
 Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo,  
 Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi,  
 Katia  
 CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici  
 Rizzoli, Bologna, 40136, Italy  
 SOURCE: Oncogene (2004), 23(33), 5664-5674  
 CODEN: ONCNES; ISSN: 0950-9232  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Connecting via Winsock to STN

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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
NEWS	9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist \$500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006

=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006  
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STRUCTURE FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1  
DICTIONARY FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> E "DOLASTATIN"/CN 25  
E1 1 DOLASETRON MESYLATE/CN  
E2 1 DOLASTANE/CN  
E3 0 --> DOLASTATIN/CN  
E4 1 DOLASTATIN 1/CN  
E5 1 DOLASTATIN 10/CN  
E6 1 DOLASTATIN 11/CN  
E7 1 DOLASTATIN 12/CN  
E8 1 DOLASTATIN 13/CN  
E9 1 DOLASTATIN 13,  
4-(3-AMINO-3,4-DIHYDRO-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN  
E10 1 DOLASTATIN 13,  
4-(3-AMINO-3,4-DIHYDRO-6-HYDROXY-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC  
ACID)-/CN

E11 1 DOLASTATIN 14/CN  
 E12 1 DOLASTATIN 15/CN  
 E13 1 DOLASTATIN 16/CN  
 E14 1 DOLASTATIN 17/CN  
 E15 1 DOLASTATIN 17 (DOLABELLA AURICULARIA)/CN  
 E16 1 DOLASTATIN 18/CN  
 E17 1 DOLASTATIN 19/CN  
 E18 1 DOLASTATIN 2/CN  
 E19 1 DOLASTATIN 3/CN  
 E20 1 DOLASTATIN 4/CN  
 E21 1 DOLASTATIN 5/CN  
 E22 1 DOLASTATIN 6/CN  
 E23 1 DOLASTATIN 7/CN  
 E24 1 DOLASTATIN 8/CN  
 E25 1 DOLASTATIN 9/CN

=> S E6

L1 1 "DOLASTATIN 11"/CN

=> DIS L1 1 SQIDE

THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

RN 111517-68-1 REGISTRY

CN Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-dimethyl-L-tyrosyl-(4S)-4-amino-2,2-dimethyl-3-oxopentanoyl] (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.

CN **Dolastatin 11**

OTHER NAMES:

CN NSC 606195

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 8

NTE modified (modifications unspecified)

type	location	description
bridge	Gly-1 - Oaa-8	covalent bridge
uncommon	Oaa-6 -	-
uncommon	Oaa-8 -	-

SEQ 1 GLGVYXAX

MF C50 H80 N8 O12

SR CA

LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

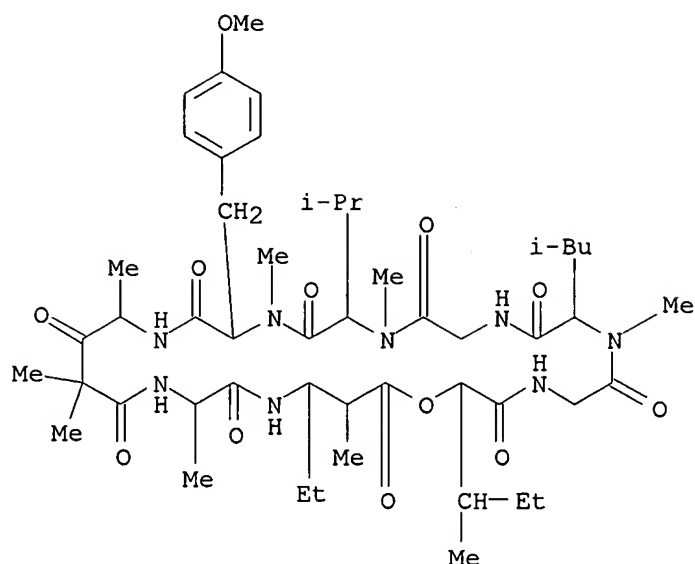
DT.CA Caplus document type: Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: PREP (Preparation); PRP (Properties)





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

22 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> DIS L1 1 SQIDE

THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS  
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:N  
 REQUEST CANCELED

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

12.00

12.21

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006

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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17

FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

```
=> s actin
      49670 ACTIN
      30327 ACTINS
L2      52669 ACTIN
        (ACTIN OR ACTINS)

=> s cofilin
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      232 COFILINS
L3      812 COFILIN
        (COFILIN OR COFILINS)
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      1822219 INHIBIT?
L4      1968300 ANTAG? OR INHIBIT?
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=> s l4 (l) l3
L5      222 L4 (L) L3
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=> s ewing?
L6      1659 EWING?
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=> s l6 and l5
L7      1 L6 AND L5
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=> d ibib
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L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention
or treatment of a tumorous state, comprising a
modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De
Cachan; Institut Gustave Roussy-IGR; Centre National
de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
FR 2825928	A1	20021220	FR 2001-7976	20010618

FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:			FR 2001-7976	A 20010618
			WO 2002-FR2106	W 20020618

=> s l1

L8 22 L1

=> s l8 and l6

L9 0 L8 AND L6

=> s zyxin

219 ZYXIN

28 ZYXINS

L10 224 ZYXIN

(ZYXIN OR ZYXINS)

=> s l10 and l6

L11 3 L10 AND L6

=> d ibib 1-3

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:184733 CAPLUS

DOCUMENT NUMBER: 142:371546

TITLE: The actin cytoskeleton-associated protein  
**zyxin** acts as a tumor suppressor in  
Ewing tumor cells

AUTHOR(S): Amsellem, Valerie; Kryszke, Marie-Helene; Hervy,  
Martial; Subra, Frederic; Athman, Rafika; Leh, Herve;  
Brachet-Ducos, Corinne; Auclair, Christian

CORPORATE SOURCE: CNRS UMR 8113, Laboratoire de Biotechnologie et  
Pharmacologie genetique appliquee, Ecole Normale  
Superieure de Cachan, Cachan, 94230, Fr.

SOURCE: Experimental Cell Research (2005), 304(2), 443-456  
CODEN: ECREAL; ISSN: 0014-4827

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:583223 CAPLUS

DOCUMENT NUMBER: 141:188806

TITLE: Molecular mechanisms of CD99-induced  
caspase-independent cell death and cell-cell adhesion  
in Ewing's sarcoma cells: actin and  
**zyxin** as key intracellular mediators

AUTHOR(S): Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania;  
Bernard, Ghislaine; Manara, Maria Cristina; Benini,  
Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi,  
Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo,  
Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi,  
Katia

CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici  
Rizzoli, Bologna, 40136, Italy

SOURCE: Oncogene (2004), 23(33), 5664-5674  
 CODEN: ONCNES; ISSN: 0950-9232  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:977858 CAPLUS  
 DOCUMENT NUMBER: 138:52333  
 TITLE: Pharmaceutical composition for diagnosis, prevention  
 or treatment of a tumorous state, comprising a  
 modulator of the actin polymerization state  
 INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial;  
 Subra, Frederic  
 PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De  
 Cachan; Institut Gustave Roussy-IGR; Centre National  
 de la Recherche Scientifique CNRS  
 SOURCE: PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:			FR 2001-7976	A 20010618
			WO 2002-FR2106	W 20020618

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006  
 E "DOLASTATIN"/CN 25

L1 1 S E6

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006  
 L2 52669 S ACTIN

L3 812 S COFILIN  
 L4 1968300 S ANTAG? OR INHIBIT?  
 L5 222 S L4 (L) L3  
 L6 1659 S EWING?  
 L7 1 S L6 AND L5  
 L8 22 S L1  
 L9 0 S L8 AND L6  
 L10 224 S ZYXIN  
 L11 3 S L10 AND L6

=> s l3 and l6

L12 6 L3 AND L6

=> s l12 and l4

L13 4 L12 AND L4

=> d ibib 1-4

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:248644 CAPLUS

DOCUMENT NUMBER: 142:274057

TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

INVENTOR(S): Liew, Choong-chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004241727	A1	20041202	US 2004-812731	20040330
PRIORITY APPLN. INFO.:			US 1999-115125P	P 19990106
			US 2000-477148	B1 20000104
			US 2002-268730	A2 20021009
			US 2003-601518	A2 20030620
			US 2004-802875	A2 20040312
			US 2004-812731	A 20040330

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:248643 CAPLUS

DOCUMENT NUMBER: 142:274056

TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004241727	A1	20041202	US 2004-812731	20040330

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812731	A	20040330

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60754 CAPLUS  
Correction of: 2004:1036571

DOCUMENT NUMBER: 142:233342  
Correction of: 142:16836

TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 29

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004265869	A1	20041230	US 2004-812716	20040330
US 2005208519	A1	20050922	US 2004-989191	20041115

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812731	A2	20040330
WO 2004-US20836	A2	20040621

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:977858 CAPLUS

DOCUMENT NUMBER: 138:52333

TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state

INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic

PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS

SOURCE: PCT Int. Appl., 68 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:				
			FR 2001-7976	A 20010618
			WO 2002-FR2106	W 20020618

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006  
E "DOLASTATIN"/CN 25

L1 1 S E6

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006

L2 52669 S ACTIN  
L3 812 S COFILIN  
L4 1968300 S ANTAG? OR INHIBIT?  
L5 222 S L4 (L) L3  
L6 1659 S EWING?  
L7 1 S L6 AND L5  
L8 22 S L1  
L9 0 S L8 AND L6  
L10 224 S ZYXIN  
L11 3 S L10 AND L6  
L12 6 S L3 AND L6  
L13 4 S L12 AND L4

=> s phosphoinositol?

L14 989 PHOSPHOINOSITOL?

=> s l14 and l6

L15 0 L14 AND L6

=> s phosphotidylinositol

96 PHOSPHOTIDYLINOSITOL  
2 PHOSPHOTIDYLINOSITOLS

L16 98 PHOSPHOTIDYLINOSITOL  
(PHOSPHOTIDYLINOSITOL OR PHOSPHOTIDYLINOSITOLS)

=> s l15 and l16

L17 0 L15 AND L6

=> file pctfull

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

29.78

41.99

FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006  
COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED: 11 APR 2006 <20060411/UP>  
MOST RECENT UPDATE WEEK: 200614 <200614/EW>  
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.

SEE

<http://www.stn-international.de/stndatabases/details/ipc-reform.html> >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE  
(last updated April 10, 2006) <<<

=> s cofilin

179 COFILIN  
12 COFILINS

L18 188 COFILIN  
(COFILIN OR COFILINS)

=> s ewing?

L19 3185 EWING?

=>

=> s l19 and l18

L20 19 L19 AND L18

=> s antag? or inhibit?

53720 ANTAG?  
189862 INHIBIT?

L21 198141 ANTAG? OR INHIBIT?

=> s l20 and l21

L22 19 L20 AND L21

=> s l22 not py>2001

488865 PY>2001

L23 4 L22 NOT PY>2001

=> d ibib 1-4

L23 ANSWER 1 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2001055168 PCTFULL ED 20020827  
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES



TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES, ET ANTICORPS  
 INVENTOR(S): ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;  
 ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055168	A1	20010802

DESIGNATED STATES  
 W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
 CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:  
 PRIORITY INFO.:

WO 2001-US1331	A	20010117
US 2000-60/179,065		20000131
US 2000-60/180,628		20000204
US 2000-60/184,664		20000224
US 2000-60/186,350		20000302
US 2000-60/189,874		20000316
US 2000-60/190,076		20000317
US 2000-60/198,123		20000418
US 2000-60/205,515		20000519
US 2000-60/209,467		20000607
US 2000-60/214,886		20000628
US 2000-60/215,135		20000630
US 2000-60/216,647		20000707
US 2000-60/216,880		20000707
US 2000-60/217,487		20000711
US 2000-60/217,496		20000711
US 2000-60/218,290		20000714
US 2000-60/220,963		20000726
US 2000-60/220,964		20000726
US 2000-60/225,757		20000814
US 2000-60/225,270		20000814
US 2000-60/225,447		20000814
US 2000-60/225,266		20000814
US 2000-60/225,213		20000814
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US 2000-60/224,519		20000814
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US 2000-60/227,182		20000822
US 2000-60/226,681		20000822
US 2000-60/227,009		20000823
US 2000-60/228,924		20000830
US 2000-60/229,344		20000901
US 2000-60/229,343		20000901
US 2000-60/229,287		20000901
US 2000-60/229,345		20000901

US 2000-60/229,513	20000905
US 2000-60/229,509	20000905
US 2000-60/230,438	20000906
US 2000-60/230,437	20000906
US 2000-60/231,413	20000908
US 2000-60/232,081	20000908
US 2000-60/231,244	20000908
US 2000-60/231,414	20000908
US 2000-60/232,080	20000908
US 2000-60/231,242	20000908
US 2000-60/231,243	20000908
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US 2000-60/233,065	20000914
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US 2000-60/232,398	20000914
US 2000-60/234,223	20000921
US 2000-60/234,274	20000921
US 2000-60/234,998	20000925
US 2000-60/234,997	20000925
US 2000-60/235,484	20000926
US 2000-60/235,834	20000927
US 2000-60/235,836	20000927
US 2000-60/236,369	20000929
US 2000-60/236,367	20000929
US 2000-60/236,368	20000929
US 2000-60/236,370	20000929
US 2000-60/236,327	20000929
US 2000-60/237,039	20001002
US 2000-60/237,038	20001002
US 2000-60/237,040	20001002
US 2000-60/237,037	20001002
US 2000-60/236,802	20001002
US 2000-60/239,937	20001013
US 2000-60/239,935	20001013
US 2000-60/241,221	20001020
US 2000-60/241,808	20001020
US 2000-60/241,787	20001020
US 2000-60/240,960	20001020
US 2000-60/241,809	20001020
US 2000-60/241,785	20001020
US 2000-60/241,786	20001020
US 2000-60/241,826	20001020
US 2000-60/244,617	20001101
US 2000-60/246,474	20001108
US 2000-60/246,532	20001108
US 2000-60/246,609	20001108
US 2000-60/246,613	20001108
US 2000-60/246,610	20001108
US 2000-60/246,611	20001108
US 2000-60/246,477	20001108
US 2000-60/246,527	20001108
US 2000-60/246,528	20001108
US 2000-60/246,525	20001108
US 2000-60/246,475	20001108
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US 2000-60/246,476	20001108
US 2000-60/246,478	20001108
US 2000-60/246,523	20001108

US 2000-60/246,524	20001108
US 2000-60/249,299	20001117
US 2000-60/249,297	20001117
US 2000-60/249,244	20001117
US 2000-60/249,245	20001117
US 2000-60/249,207	20001117
US 2000-60/249,212	20001117
US 2000-60/249,213	20001117
US 2000-60/249,208	20001117
US 2000-60/249,218	20001117
US 2000-60/249,215	20001117
US 2000-60/249,211	20001117
US 2000-60/249,217	20001117
US 2000-60/249,216	20001117
US 2000-60/249,210	20001117
US 2000-60/249,214	20001117
US 2000-60/249,264	20001117
US 2000-60/249,265	20001117
US 2000-60/249,300	20001117
US 2000-60/249,209	20001117
US 2000-60/250,160	20001201
US 2000-60/250,391	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 1999051766 PCTFULL ED 20020515  
 TITLE (ENGLISH): METHODS FOR PRODUCING LIBRARIES OF EXPRESSIBLE GENE SEQUENCES  
 TITLE (FRENCH): METHODES DE PRODUCTION DE BANQUES DE SEQUENCES DE GENES EXPRIMABLES  
 INVENTOR(S): FERNANDEZ, Joseph, Manuel;  
 HEYMAN, John, Alastair;  
 HOFFLER, James, Paul;  
 MARKS-HULL, Heather, Lynn;  
 SINDICI, Michelle, Lynn  
 PATENT ASSIGNEE(S): INVITROGEN;  
 FERNANDEZ, Joseph, Manuel;  
 HEYMAN, John, Alastair;  
 HOFFLER, James, Paul;  
 MARKS-HULL, Heather, Lynn;  
 SINDICI, Michelle, Lynn  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951766	A1	19991014

DESIGNATED STATES  
 W: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU  
 MC NL PT SE  
 APPLICATION INFO.: WO 1999-US7270 A 19990402  
 PRIORITY INFO.: US 1998-09/054,936 19980403

L23 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN  
 1999051620 PCTFULL ED 20020515  
 ACCESSION NUMBER:  
 TITLE (ENGLISH): LIBRARIES OF EXPRESSIBLE GENE SEQUENCES  
 TITLE (FRENCH): BANQUES DE SEQUENCES DE GENES POUVANT ETRE EXPRIMEES  
 INVENTOR(S): FERNANDEZ, Joseph, Manuel;  
 HEYMAN, John, Alastair;  
 HOEFFLER, James, Paul  
 PATENT ASSIGNEE(S): INVITROGEN  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951620	A1	19991014

DESIGNATED STATES  
 W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC  
 NL PT SE

APPLICATION INFO.: WO 1999-US7334 A 19990402  
 PRIORITY INFO.: US 1998-60/080,626 19980403  
 US 1998-60/096,981 19980818

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN  
 1998041648 PCTFULL ED 20020514  
 ACCESSION NUMBER:  
 TITLE (ENGLISH): TARGET GENES FOR ALLELE-SPECIFIC DRUGS  
 TITLE (FRENCH): GENES CIBLES POUR MEDICAMENTS SPECIFIQUES D'ALLELES  
 INVENTOR(S): HOUSMAN, David;  
 LEDLEY, Fred, D.;  
 STANTON, Vincent, P., Jr.  
 PATENT ASSIGNEE(S): VARIAGENICS, INC.;  
 HOUSMAN, David;  
 LEDLEY, Fred, D.;  
 STANTON, Vincent, P., Jr.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841648	A2	19980924

DESIGNATED STATES  
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
 ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS  
 LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG  
 SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW AT BE CH DE  
 DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1998-US5419 A 19980319  
 PRIORITY INFO.: US 1997-60/041,057 19970320

=> d kwic 2

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . U3 52.36 60  
 snoRNP associated 55 kDa  
 protein  
 GI H-DO0096 Transthyretin (prealbumin) 16.28 20  
 C4 H-DO0408 Cytochrome P450 IIIA7 (P450- 55.44 64  
 HFLa)  
 M302 E7 H-DO0682 **cofilin** 18.37 30  
 M383 G2 H-DO0726 ferrochelatase 46.64 50.OkDa  
 M383 C3 H-DO0760 proteasome, subunit HO 25.85 34.OkDa  
 M305 B4 H-DO0761 proteasome, subunit HC5 26.62. . .  
 . . .

enoyl-Coenzyme A hydratase, 32.01 58  
 short chain, mitochondrial  
 E1 H-DI4446 Human HFREP- I mRNA for 34.43 40  
 unknown protein, complete cds  
 167-14 H-DI4497 H.sapiens (**Ewing's** sarcoma cell 51.44 64  
 line) mRNA encoding open  
 reading frame  
 M266 D2 H-DI4520 basic transcription element- 24.2 33.OkDa  
 binding protein 2  
 M318 D2 H-DI4658 hypothetical. . .  
 .  
 .  
 42.79 48  
 M298 C2 H-JO2611 apolipoprotein D 20.9 3 I.OkDa  
 M266 C4 H-JO2683 ADP/ATP carrier protein 32.89 36  
 M383 H2 H-JO2685 plasminogen activator **inhibitor**, 45.76  
 50.OkDa  
 placenta  
 167-3 H-JO2853 casein kinase 11, alpha chain 43.08 50  
 E3 H-JO2854 Human 20-kDa myosin light 19.03 31  
 chain (MLC-2) mRNA, complete  
 cds  
 M248. . .  
 .  
 .  
 transaldolase 37.18 39.OkDa  
 M423 C4 H-LI9593 Interleukin 8 receptor, beta 39.71 4 1.0kDa  
 G I H-LI9686 Homo sapiens macrophage 12.76 1 3  
 migration **inhibitory** factor (MIF)  
 gene, complete cds  
 G2 H-LI9739 metallopanstimulin 1 9.35 32  
 M302 E3 H-LI9871 activating transcription factor 3 20.02 36.OkDa  
 167-86 H-L20422 14 3 protein eta 34 1 3  
 M440 B2 H-L20492 Human gamma-glutamyl 24.86 35.OkDa  
 transpeptidase mRNA, complete  
 cds  
 M315 BI H-L20688 GDP-dissociation **inhibitor** 22.22 32  
 protein rhoA  
 M271 H3 H-L20941 ferritin, heavy polypeptide. 20.24 32  
 FERRITIN IS AN  
 INTRACELLULAR,  
 MOLECULE THAT STORES  
 IRON IN A SOLUBLE,  
 NONTOXIC, READILY  
 AVAILABLE FORM.  
 .  
 .  
 30  
 transforming protein rhoC,  
 Aplysia ras-related homolog 9  
 M236 E3 H-L25085 Sec61 complex, beta subunit, 10.67 19  
 PROTEIN TRANSLOCATION  
 TN THE ENDOPLASMIC  
 RETICULUM  
 167-85 H-1,25610 cyclin-dependent kinase **inhibitor** 32  
 B2 H-L25610 cyclin-dependent kinase **inhibitor** 18.110 40  
 1  
 M297 H2 H-1,26232 cathepsin A/phospholipid transfer 54.34 64.OkDa  
 protein  
 167-4 H-1,26318 stress-activated protein kinase 52 42.31  
 JNKI  
 M428 F1 H-1,27586 Human TR4 orphan. . .  
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 E2 H-MI9713 tropomyosin, alpha, muscle 31.35 4I.OkDa  
 167-79 H-MI9722 proto-oncogene tyrosine-protein 64 58.26  
 kinase FGR

M248 HI H-M20560 Annexin III (lipocortin III), 35.64 37  
**INHIBITOR OF**  
PHOSPHOLIPASE A2  
M235 HI H-M20681 GLUCOSE TRANSPORTER 54.67 50  
TYPE 3, BRAIN  
167-29 H-M21616 beta platelet-derived growth 121 121.7  
factor receptor precursor  
M305 A3 H-M21812. . .  
. . .  
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erythrocyte, 55 kDa  
M302 C7 H-M65292 complement factor H-related 36.41 50  
protein (GB:M65292)  
D3 H-M68516 Human protein C **inhibitor** gene, 44.77 54  
complete cds  
167-27 H-M68520 cell division protein kinase 2 38 32.85  
M236 D5 H-M68867 Cellular retinoic acid-binding 15.29 19.OkDa  
protein 2,. . .  
. . .  
A1 H-PO 197 S-adenosynmethionine synthetase 42.46  
2 (metX)  
M365 BI H-PO203 hypothetical protein 10.12  
M365 C1 H-PO209 hypothetical protein 49.61  
M365 DI H-PO213 glucose **inhibited** division protein 68.42  
(gidA)  
M381 E1 H-PO218 hypothetical protein 20.24  
M365 E1 H-PO221 nifLJ-Iike protein 35.97  
M365 F1 H-PO227 outer m mbrane protein (omp5). . . C2 P]3 -]]  
ribosomal protein SI (rps 1)  
M366 D2 H-PO403 phenylalanyl-tRNA synthetase, 36.19  
alpha subunit (pHeS)  
M366 E2 H-PO404 protein kinase C **inhibitor** 11.55  
(SP:PI6436)  
M366 F2 H-PO405 nifS-like protein 48.51  
M366 G2 H-PO406 hypothetical protein 21.67  
M366 H2 H-PO407 biotin sulfoxide reductase (bisC) 87.67  
M381 DI H-PO409. . .  
. . .  
alanine racemase, biosynthetic 41.58  
(a  
M371 D6 H-PO942 D-alanine glycine perinease 49.61  
(dagA)  
M371 E6 H-PO943 D-arnino acid dehydrogenase 45.21  
(dadA)  
M371 F6 H-PO944 translation initiation **inhibitor**, 13.86  
putative  
M371 G6 H-PO946 conserved hypothetical integral 54.67  
membrane protein  
M371 H6 H-PO947 hypothetical protein 13.31  
M371 A7 H-PO949 conserved hypothetical secreted 16.61  
protein  
M371 B7. . .  
. . .  
factor Ile, 48.360  
alpha subunit  
M302 D7 H-S69022 myosin, light polypeptide 2, 18.26 3 1  
ventricular  
H5 H-S69272 cytoplasmic antiproteinase=38 41.47 50  
kda intracellular serine proteinase  
**inhibitor** [human, placenta,  
mRNA, 1465 nt]  
DI H-S72043 GIF=growth **inhibitory** factor 7.59 19  
[human, brain, Genornic, 2015 nt]

M266 B3 H-S74221 cytokine lK factor 17.93 36.OkDa  
DI H-S74445 cellular retinoic acid-binding 15.18 23  
protein. . . small nuclear ribonucleoprotein, 13.97 17.OkDa  
Sm D3  
M311 D4 H-UI6660 enoyl-Coenzyme A hydratase-like 36.19 38  
protein, peroxisomal  
M302 H4 H-UI7074 cyclin-dependent kinase 6 18.59 29  
**inhibitor** p 1 8  
M306 A2 H-UI7195 A-kinase anchor protein I 00 72.05 100  
[AKAPI00\*]  
DI -UI7280 Steroidogenic acute regulatory 31.46 35  
protein  
M316 171 H-UI8291. . .  
. . .  
29.15 38.OkDa  
factor TAF1132 mRNA, complete  
cds  
M424 H3 H-U22662 Human nuclear orphan receptor 49.28 49.OkDa  
LXR-alpha mRNA, complete cds  
M271 D2 H-U24074 killer cell **inhibitory** receptor 37.62 43  
[KIR], Homo sapiens natural  
killer-associated transcript 3  
(NKAT3), complete cds.  
. . .  
30  
gamma  
M416 D3 H-U26403 Human receptor tyrosine kinase 25.19 30.OkDa  
ligand LERK-7 precursor  
(EPLG7) mRNA, complete cds  
M317 E2 H-U27143 human protein kinase C **inhibitor**- 13.900  
17.OkDa  
I cDNA  
E5 H-U28249 Human II kd protein mRNA, 12.32 12  
complete cds  
F4 H-U28386 Human nuclear localization 58.3 54  
sequence receptor hSRP. . . phosphatase 2A, 56.65 55.OkDa  
regulatory subunit B' alpha- I  
E1 H-U37529 Human substance P beta-PPT-A 14.3 22  
mRNA, complete cds  
M305 H5 H-U37547 apoptosis **inhibitor** 68.09 64  
M424 D5 H-U38480 Human retinoid X receptor- 51.04 61.OkDa  
gamma mRNA, complete cds  
M270 F4 H-U38810 Human mab-21 cell fate-  
determining protein. . . mRNA  
M298 E4 H-U39945 human adenylate kinase 2 (adk2) 26.3633 38.OkDa  
mRNA  
166-38 H-U40282 human integrin-finked kinase 55 49.68  
(ILK) mRNA  
169-65 H-U40343 human CDK **inhibitor** p I 9INK4d 1 8 18. 33  
mRNA  
E2 H-U40705 Homo sapiens telomeric repeat 48.4 52  
binding factor (TRF I) mRNA,  
complete cds  
166-50 H-U40989. . . E2 H-U47677 Human transcription factor E2F 1  
48.18 53.OkDa  
(E2FI) gene, promoter and  
m421 H I H-U48707 Human protein phosphatase- 1 18.92 36.OkDa  
**inhibitor** mRNA, complete cds  
M302 B7 H-U49070 peptidyl-prolyl isomerase PIN I 18.04 28.OkDa  
C1 H-U49188 Human placenta (Diff33) mRNA, 54.45 70  
complete cds  
M485 H2. . .  
. . .

46.97 60.OkDa  
 phosphodiesterase (PDE4Q  
 mRNA, 4C-426 isoform,  
 complete cds  
 M306 F3 H-U66867 ubiquitin-conjugating enzyme E21 17.49 28  
 [UBE2I]  
 M416 E2 H-U681 11 Human protein phosphatase 22.66 37.OkDa  
   **inhibitor** 2 (PPP I R2) gene  
 F2 H-U68382 Mannosidase, alpha B, lysosomal 35.64 36  
 G2 H-U69141 Glutaryl-Coenzyme A 48.29 56  
 dehydrogenase  
 B2 H-U70660 Human copper. . . (HAHI) mRNA, complete  
 cds  
 M297 B2 H-U71374 peroxisomal membrane protein 40.15 40.OkDa  
 (Pex13p)  
 M306 A3 H-U75272 progastricsin [PGC] 42.79 49.OkDa  
 A2 H-U75285 Homo sapiens apoptosis **inhibitor** 15.73 25  
 survivin gene, complete cds  
 B2 H-U77456 Human nucleosome assembly 41.36 50  
 protein 2 mRNA, complete cds  
 C2 H-U78294 Homo sapiens 15S-lipoxygenase 74.47. . . and VIIIA)  
 M302 B3 H-XO2751 proto-oncogene N-ras 20.9 25.OkDa  
 D3 H-XO2812 Human mRNA for transforming 43.12 50  
 growth factor-beta (TGF-beta)  
 M302 CI H-XO3124 tissue **inhibitor** of 22.88 T6.OkDa  
 metalloproteinase I  
 M362 BI H-XO3342 ribosomal protein L32 14.96 24.OkDa  
 M235 A2 H-XO3484 human mRNA for raf oncogene 71.350 73.OkDa  
 M318. . .  
 .  
 .  
 basic protein, 23 kDa 22.44 30.OkDa  
 M318 GI H-X57025 insulin-like growth factor 1 16.94 1 8  
 M305 F5 H-X57348 protein kinase C **inhibitor** 27.39 35.OkDa  
 M236 D6 H-X57351 interferon-induced protein 1-813 14.63 24  
 H3 H-X57352 interferon-induced protein 1-8U 14.74 38  
 M305 B6 H-X58079 S- I 00. . . 49  
 E2 H-X59357 Epstein-Barr virus small RNA- 14.19 36  
 associated protein  
 M236 D4 H-X59417 macropain, iota subunit, THE 27.17 36  
 INTERACTION OF CALPONIN  
 WITH ACTIN **INHIBITS**  
 ACTOMYOSIN MG-ATPASE  
 ACTIVITY  
 M271 H4 H-X59618 ribonucleotide reductase, small 42.9 46  
 subunit  
 M250 G3 H-X59710 CAAT-box DNA-binding protein, 22.66 34  
 subunit B, CCAAT-BINDING  
 TRANSCRIPTION FACTOR  
 SUBUNIT A [Homo. . .  
 .  
 .  
 H+ transporting, 42.13 58.OkDa  
 subunit C, vacuolar  
 M236 C3 H-X69392 ribosomal protein L26 16.06 29  
 B3 H-X69532 H.sapiens gene for inter-alpha- 100.32 98  
 trypsin **inhibitor** heavy chain HI,  
 exons 1-3  
 M236 F5 H-X69654 ribosomal protein S26 12.76 18  
 M421 C8 H-X70218 Protein phosphatase 4 (formerly 33.88  
 X), catalytic subunit  
 M266. . .  
 .  
 M235 BI H-X72841 Human retinoblastoma-binding 46.86 52.OkDa  
 protein (RbAp46) mRNA,



complete cds, IEF 7442  
 (GB:X72841)  
 217-25 H-X73428 DNA-binding protein **inhibitor** 20 17.08  
 ID-3  
 M305 B5 H-X73459 signal recognition particle, 15.07 20  
 subunit 14  
 M250 D6 H-X73460 ribosomal protein L3, isoform 2, 44.44 50.OkDa  
 COMPONENT OF. . .

H-YO0291 Human hap mRNA encoding a 49.39 59.OkDa  
 DNA-binding hormone receptor  
 M386 HI H-YO0345 polyadenylate-binding protein 69.74 70.OkDa  
 M469 A2 H-YO0630 Plasminogen activator **inhibitor**, 45.76  
 46.OkDa  
 type II (arginine-serpin)  
 M305 EI H-YO0711 lactate dehydrogenase B 36.85 38.OkDa  
 H2 H-YO0764 ubiquinol/cytochrome c reductase 10.12 33  
 hinge protein  
 F5 H-YO7848 H.sapiens. . .

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ABEN . . .  
 loss of one of these alleles in cancer cells due to loss of  
 heterozygosity (LOH) and (2) the  
 development of **inhibitors** with high specificity for the single  
 remaining alternative allele of the  
 essential gene retained by the tumor cell after LOH.. . .

ABFR . . . perte de l'un de ces alleles dans des cellules cancéreuses, due a  
 la perte  
 d'hétérozygotie (LOH); et (2) développer des **inhibiteurs**  
 présentant une spécificité élevée pour  
 l'allele distinct restant du gene essentiel retenu par la cellule  
 tumorale apres LOH. Des categories. . .

DETD Specifically, this invention is concerned with target genes for drugs  
 that are useful  
 for treating such diseases by providing allele-specific  
**inhibition** of essential cell  
 functions.

. . .  
 strategy for the development of anticancer agents having a high  
 therapeutic  
 232/116  
 index is described in Housman, International Application PCT/US/94 08473  
 and  
 Housman, **INHIBITORS** OF ALTERNATIVE ALLELES OF GENES  
 ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH  
 AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S.. . . which undergo  
 loss of  
 heterozygosity in a cancer. Treatment of a cancer in an individual who  
 is  
 heterozygous with an allele specific **inhibitor** targeted to the  
 single allele of an  
 essential gene which is present in a cancer will **inhibit** the  
 growth of the cancer  
 cells. In contrast, the alternative allele present in non-cancerous  
 cells (which have  
 not undergone loss of heterozygosity). . .

. . .  
 (3) identification of the absence of one of these alleles in

cancer cells due to LOH and (4) development of specific **inhibitors** of the single remaining allele of the essential gene retained by the cancer cell, but not the alternative allele.

#### SUMMARY OF THE INVENTION

The utilization of **inhibitors** of alternative alleles, such as in the strategy described in Housman, supra, requires the provision of suitable target genes in order to identify such **inhibitors** and to implement corresponding diagnostic or therapeutic methods. Thus, as described below, the present invention identifies useful groups of genes which provide. . .

In each disease, the administration of such an **inhibitor** would have cytotoxic or antiproliferative effects on the abnormally proliferating cells that exhibited LOH and contained only the sensitive allele of the. . .

In addition, it was found that specific **inhibitors** of alternative alleles of an essential gene would be useful in managing transplantation in instances where the alleles in a donor bone marrow differ from the alleles in the recipient. For example, administration of an **inhibitor** of an allele that was present in a donor bone marrow but not the recipient could be used to treat graft-versus-host. . .

Alternatively, an **inhibitor** of an allele that is present in the recipient but not the donor bone marrow could be used to enhance engraftment by preferentially creating space in the recipient bone marrow for the graft without **inhibiting** proliferation of the engrafted donor marrow.

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The term target gene refers to a gene where the gene, its RNA transcript, or its protein product are specifically **inhibited** or potentially **inhibited** by a drug. In references herein to genes or alleles, the term encoding refers to the entire gene sequence, including both coding. . .

. . . of alternative variances at a single variant site, or a combination of several different variances at different sites. In this invention, **inhibitors** targeted to a specific allelic form or subset of the allelic forms of a gene can be targeted to a specific variance. . .

. . . dysplastic epithelium of lung, breast, cervix, or other tissues. Drugs used in treating cancer and other non-cancer proliferative disorders commonly aim to **inhibit** the proliferation of cells and are commonly referred to as antiproliferative agents.

particular sequence variance. Also preferably, these terms refer to loss of heterozygosity of a particular sequence variance that is recognized by an **inhibitor** that will **inhibit** one allele of the gene present in normal cells of the individual, but not an alternative allele.

the individual clones. The alleles subject to LOH may vary from one clone to another. Therefore treatment of these conditions preferably utilizes

**inhibitors** of at least two allelic forms. Thus, methods relating to such disorders can utilize alternative alleles of one gene and/or allelic. . .

of LOH in certain locations, for example segments of chromosomes 7,8,10,11,13,16, and 18 in prostate cancer, administration of an allele-specific drug that **inhibits** one allele that is within such a region, in a patient who is heterozygous for alternative forms of the gene, would. . .

genes, and provides, as examples, specific genes within those categories which are found to be suitable as targets for allele specific **inhibitors**, in particular for killing cancer cells or reducing the proliferation of cells in cancer or noncancer proliferative disorders. Thus, the present invention. . . more variant positions, indicates that the gene is a useful potential target gene in this invention for the identification of allele specific **inhibitors** and in other aspects of the invention.

those skilled in the art) identifying the gene and providing a known sequence) which can be used for identifying allele specific **inhibitors** and for use in other aspects of this invention. Preferably the gene has the LOH frequency and at least one sequence variance. . .

vital for cell viability or growth, or essential for cell survival and proliferation have the same meaning. A gene is essential if

**inhibition** of the function of such a gene or gene product will kill the cell or **inhibit** its growth as determined by methods known in the art. Growth **inhibition** can be monitored as a reduction or preferably a cessation of cell proliferation.

the affected gene, genetic disruption of the gene by homologous recombination or other methods in organisms ranging from yeast to mice, **inhibition** of the gene by antisense oligonucleotides or ribozymes, and identification of the target of known cytotoxic, drugs and other **inhibitors**. As further discussed below, the essentiality of a gene can depend on the conditions to which the cell is

exposed.

entity is absent or present at low levels, the gene product is essential. In another example, the administration of a drug that

**inhibits** one or more functions within the cell can cause other functions to be essential that are not essential in the absence. . .

Identification of one or more sequence variances in that gene and/or in the corresponding gene products allows screening or design of such **inhibitors** for potential treatment.

sequence variance, and therefore of individuals heterozygous for such variances, indicates that the gene can be used for the identification of **inhibitors** targeting allelic forms of the gene which have a particular variance or variances and in the other aspects of this invention.

gene is a potential target. The target gene, its RNA transcript or protein product can then be used as targets for allele-specific **inhibitors** for treating the proliferative disorder or other uses as described in the aspects of this invention.

of the population are heterozygous for that gene provides genes which are particularly likely to be useful target genes for allele specific **inhibition** in this invention.

or 50% of cases of such a disorder indicates that the gene is useful as a potential target for identifying allele specific

**inhibitors** for the treatment of proliferative disorders and in other aspects of this  
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invention.

more preferably at least 30%, and most preferably at least 40% are heterozygous in a specific population that may be treated with **inhibitors** to treat cancer or other proliferative disorder in that population. Once a specific variance is identified in a certain gene, the. . .

In the context of this invention, an alternative allele, or other reference to an appropriate target for the **inhibitors** of this invention refers to a form of a gene which differs in base sequence from at least one other allele or. . . no phenotypic effect on the physical condition of an individual having that variance until the variance is targeted by an allele specific **inhibitor**.

In connection with allele specific **inhibitors** and the methods of this invention, the

terms allelic form or alternative form of the target gene or sequence variance within the. . . either or both of the gene or a product of that gene including the RNA transcript or protein product. Thus, a particular

**inhibitor** may act in an allele specific manner (which will often be variance specific) at any of those levels and preferably the **inhibitor** is targeted to a particular sequence variance of the specific allelic form.

the classes described above in genes that are essential for cell survival or proliferation that can be the targets for allele-specific **inhibitors** for the treatment of cancer or noncancer proliferative disorders.

This invention provides **inhibitors** which are specific for at least one, but not all, allelic forms of a gene that encodes a gene product essential to cell growth or cell viability, for genes belonging to the specified categories of genes. The **inhibitor** may be active on the gene or gene product including the RNA transcript, protein product, or modifications thereof. Exposure to the **inhibitor** **inhibits** proliferation or kills cells which have undergone LOH of genes that are not **inhibited** by the drug and contain only an allelic form of the essential gene, its RNA transcript, or its protein product against which the **inhibitor** is targeted. Normal cells which contain two alternative alleles of the target genes, one of which is not **inhibited** by the specific **inhibitor**, are spared from the toxic effects of the **inhibitor** because the remaining activity of the allele which is not **inhibited** by the **inhibitor** is adequate to permit continued cell viability and growth. This differential effect of the

**inhibitor** on cells with LOH of a targeted gene (e.g., a cancer cell) and normal cells accounts for the high therapeutic index of the **inhibitors** of this invention for the treatment of cancer or non-cancerous, proliferative disorders characterized by LOH. Toxicity of the **inhibitor** to normal cells is therefore low, compared to most currently available anticancer and antiproliferative agents.

indicated above and described in the Detailed Description of the Preferred Embodiments, in a first aspect the invention provides methods for identifying **inhibitors** potentially useful for treatment of a proliferative disorder, e.g., cancer. Such **inhibitors** are active on

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specific allelic forms of target genes as identified herein. The method involves determining at least two allelic forms of such a gene encoding an essential gene product, and testing a potential allele specific **inhibitor** to

determine whether the potential **inhibitor** is active on, e.g., **inhibits** expression of, at least one of the allelic forms, but not all of those forms. If the potential **inhibitor** **inhibits** only a subset of the allelic forms of the particular essential gene, then it is an allele specific **inhibitor**. Preferably the difference in activity of the **inhibitor** for different allelic forms is between allelic forms which have a sequence variance at a particular site.

In many, or even most, cases an allele specific **inhibitor** discriminates between two allelic forms due to a particular single sequence variance between the allelic forms of the target gene. For example, . . . not affect the cleavage. In the Detailed Description of the Invention specific examples of proteins, small molecules, and oligonucleotides providing allele specific **inhibition** based on single sequence variances are described. Thus, in preferred embodiments an allele specific **inhibitor** discriminates between two allelic forms by discriminating a single sequence variance. As previously indicated, **inhibitors** can be targeted to either the nucleic acid or a polypeptide (where a nucleotide change results in an amino acid change).

In particular embodiments, the allele specific **inhibitor** will recognize more than one linked sequence variances within a specific allele.

An allele specific **inhibitor** or variance specific **inhibitor** is a drug or **inhibitor** that **inhibits** the activity of one alternative allele of a gene to a greater degree than at least one other alternative allele. The difference in activity is commonly determined by the dose or level of a drug required to achieve a quantitative degree 232/116 of **inhibition**. A commonly used measure of activity is the IC50 or concentration of the drug required to achieve a 50% reduction in the measured activity of the target gene. Preferably an allele specific **inhibitor** will have at least twice the activity on the target allelic form than on a non-target allelic form, more preferably at least . . . most preferably at least 100 times. This can also be expressed as the sensitivities of the different allelic forms to the **inhibitor**.

it is equivalent to state that the target allelic form is most preferably at least 100 times as sensitive to the **inhibitor** as a non-target allelic form. The activity of an **inhibitor** can be measured either in vitro or in vivo, in

assay systems that reconstitute the in vivo system, or in systems incorporating selected elements of the complete biological system. For use in **inhibiting** cells containing only the target allelic form rather than cells containing at least one non-targeted allelic form, the difference in activity. . .

In a related aspect, the invention provides **inhibitors** potentially useful for tumor, e.g. . cancer treatment, or treatment of other proliferative disorders. Such

**inhibitors** are active on a specific allele of a gene which has at least two different alleles encoding an essential gene product in one of the target gene categories above. Such **inhibitors** can, for example, be identified by the above screening methods.

In a related aspect, the invention provides methods for producing **inhibitors** active on such specific allelic forms of belonging to one of the above categories genes by 232/116 identifying a gene encoding an essential. . . product which has alternative allelic forms in a non-tumor cell and which undergoes LOH in a tumor cell, screening to identify an **inhibitor** which is active on at least one but less than all of the alleles of the gene, and synthesizing the **inhibitor** in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a tumor in which tumor cells have only the allele on which the **inhibitor** is active.

In the context of this invention, the term active on an allelic form or allele specific **inhibitor** or specific for an allelic form indicates that the relevant

**inhibitor inhibits** an allele having a particular sequence to a greater extent (preferably > 2x) than an allele having a sequence which differs in a particular manner. Thus, for alleles for which a particular base position is identified, the

**inhibitor** has a higher degree of **inhibition** when a certain base is in the specified position than when at least one different base is in that position. This. . . means that for substitution at a particular base position, at least two of the possible allelic forms differ in sensitivity to an **inhibitor**. Usually, however, for a specific sequence variance site, the site will be occupied by one of only two bases.

Further, if an **inhibitor** acts at the polypeptide level, and any of three bases may be present at a particular position in a coding sequence but only one of the

substitutions results in an amino acid change, then the activity of the **inhibitor** would be expected to be the same for the two forms producing the same amino acid sequence but different for the form. . .

The term less active indicates that the **inhibitor** will **inhibit** growth of or kill a cell containing only the allelic form of a gene on which the **inhibitor** is more active at concentrations at which it does not significantly **inhibit** the growth of or kill a cell containing only an allelic form on which the **inhibitor** is less active.

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The term drug or **inhibitor** refers to a compound or molecule which, when brought into contact with a gene, its RNA transcript, or its gene product which the compound **inhibits**, reduces the rate of a cellular process, reduces the level of a cellular constituent, or reduces the level of activity of. . . the term to those skilled in the art and not limiting. Thus, the term generally indicates that a compound has an **inhibitory** effect on a cell or process, as understood by those skilled in the art. Examples of **inhibitory** effects are a reduction in expression of a gene product, reduction in the rate of catalytic activity of an enzyme, and reduction. . . formation or the amount of an essential cellular component. The blocking or reduction need not be complete, in most cases, for the **inhibitor** to have useful activity. Thus, in the present invention,

**inhibitors** are targeted to genes, their RNA transcript, or their protein product that are essential for cell viability or proliferation. Such **inhibitors** would have the effect of **inhibiting** essential functions, leading to loss of cell viability or **inhibition** of cell proliferation. In preferred embodiments, such **inhibitors** cause cell death or stop cell proliferation. In preferred embodiments of this invention, **inhibitors** specifically include a molecule or compound capable of **inhibiting** one or more, but not all, alleles of genes, their RNA transcript, or their protein product that are essential for cell survival or proliferation. The terms **inhibitor** of a gene or

**inhibitor** of an allele as used herein include **inhibitors** acting on the level of the gene, its gene product, its RNA transcript, its protein product, or modifications thereof and is explicitly not limited to those **inhibitors** or drugs that work on the gene sequence itself.

Several types of **inhibitors** are generally recognized in the art. A competitive

**inhibitor** is one that binds to the same site on the gene, its



RNA transcript or gene product as a natural substrate. . . is required for the action of the gene or gene product, and competitively prevents the binding of that substrate. An

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66 allosteric **inhibitor** is one that binds to a gene or gene product and alters the activity of the gene or gene product without preventing binding of a substrate or cofactor. **Inhibition** can also involve reducing the amount of the gene, RNA transcript, or its protein product, and thus the total amount of activity from the gene in the cell. Such **inhibition** can occur by action at any of a large number of different process points, including for example by **inhibiting** transcription or translation, or by inducing the elimination of the gene, its RNA transcript, or its protein product where elimination may involve. . . of the target or egress or export from the compartment in which it is active and the process of excretion or export. **Inhibition** can also be achieved by modifying the structure of the target, interfering with secondary modifications, or interfering with cofactors or other ancillary components which are required for its activity. **Inhibitors** can be comprised of small molecules or polymeric organic compounds including oligopeptides or oligonucleotides.

The term active on a gene or targeted to a gene indicates that an **inhibitor** exerts its **inhibitory** effect in a manner which is preferentially linked with the characteristic properties of a gene, its RNA transcript or its gene. . . RNA with other cellular constituents (RNA, protein, cofactors, substrates, etc.) required for activity. Thus, in general these terms indicate that the **inhibitor** acts on the gene, its RNA transcript, its protein product, its gene product, or modifications thereof, or on a reaction or reaction. . .

. . . from one of the above categories has undergone loss of heterozygosity. The method involves administering a therapeutic amount of an allele specific **inhibitor** of such an essential gene to a patient whose normal somatic cells are heterozygous for that gene but whose tumor cells contain only a single allelic form of the gene. The

**inhibitor** is active on the specific allele of the gene present in the tumor cells.

. . . cancer. The method involves administering to a patient having a precancerous condition or an early stage cancer or cancers an allele specific

**inhibitor** targeted to an allele of an essential gene for which the normal somatic cells of the patient are heterozygous and which. . . the

precancerous condition are not clonal from a single cell, the method involves subsequently administering to the patient a second allele specific **inhibitor** in an amount sufficient to **inhibit** and preferably kill cells with LOH in which an allele not targeted by the first **inhibitor** is the only remaining allele of the gene. In most cases, the second allele specific **inhibitor** will target the alternative allele of the gene targeted by the first **inhibitor**. However, the second **inhibitor** can also target an allele of a second essential gene which has undergone LOH. The second gene may have undergone LOH in. . . affected the first gene due to their proximity on a chromosome, though this is not essential. Additionally, in other cases, allele specific **inhibition** of one of the alleles of each of 3, 4, or even 232/116 more target genes can be utilized in a serial. . . genes need not be tightly linked so that LOH of the various genes does not necessarily occur together. By using the serial **inhibition** of an allele of each of the target genes, it is possible to **inhibit** and preferably kill the full population of precancerous cells in which LOH has occurred. Thus, the net effect is essentially the same as if allele specific **inhibitors** of each of the two alternative alleles of one essential gene had been used.

In the context of the administration of multiple allele specific **inhibitors**, the terms serial or subsequently indicates that the administration of two or more **inhibitors** is sufficiently temporally separated so that normal somatic cells remain functional and are therefore able to survive and/or proliferate. Those skilled. . . that the required time will depend on various factors, such as clearance rate, type and extent of the effect of an **inhibitor** on normal cells, and additive cellular toxicity, and that appropriate timing can be routinely determined for particular selections of compounds.

In another related aspect, the invention provides a method for identifying a potential patient for treatment with an **inhibitor** active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient having. . . the neoplastic cells contain only a single allele of the gene, then the patient is a potential patient for treatment with the **inhibitor**.

With respect to identifying patients with precancerous or oligoclonal proliferative 232/116 diseases characterized by LOH, and selecting appropriate allele or variance-

specific **inhibitors** for such patients, in some cases it may not be practical to obtain samples of all proliferative lesions for LOH assays... . . . aorta cannot routinely be sampled by biopsy, and dysplastic lesions in the cervix, colon, or bronchus can be multifocal. Therefore, allele specific

**inhibitors** can be selected for such conditions based on previously established patterns of LOH for the condition, and on specific testing for. . . .

most preferably 100%. However, it is not necessary that 100% of lesions show LOH for a successful treatment by allele specific **inhibitors** because 2,3,4, or even more **inhibitors** can be used in a combined approach to target an ever higher fraction of lesions, and because substantial therapeutic benefit may be achieved by **inhibiting** the proliferation of less than 100% of lesions.

In another aspect, the invention provides a method for identifying a potential patient undergoing transplantation for treatment with an **inhibitor** active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient undergoing. . . .

related aspect, the invention provides a method for treating graft versus host disease in allogenic transplantation in which an allele specific **inhibitor** is used to

**inhibit** proliferation of donor cells, e.g. . to **inhibit** stimulation of the donor immune system. In preferred embodiments, the allele specific **inhibitor** is selected by identifying alternative variances or allelic forms of an essential gene that are present in the donor tissues but not the recipient. Therapy with a variance or allele specific **inhibitor** or **inhibitors** that recognizes both alleles of the essential gene that are present in the donor, but not both alleles of the same. . . .

another aspect, the invention provides a method for enhancing engraftment of an allogenic bone marrow transplant in which an allele specific **inhibitor** is used to kill or suppress the patient's own bone marrow, providing space for engraftment of the donor cells within the marrow cavity. In preferred embodiments, the allele specific **inhibitor** is selected by identifying alternative forms of an essential gene that are present in the recipient but not the donor marrow. Therapy with an allele specific (generally a variance specific) **inhibitor** that recognizes both forms of the essential gene that are present in the recipient, but not both forms of the same gene. . . .

Allele specific **inhibitors** can be used to treat or prevent chimerism by selectively

killing or suppressing proliferation of the patient's own cells without toxicity. . .

aspect, the invention provides a method for treating cancer in a patient receiving allogenic or autologous transplantation in which an allele specific

**inhibitor** is used to kill or **inhibit** the growth of cancer cells without toxicity to the transplanted marrow. In one embodiment, in an autologous, transplantation the allele specific **inhibitor** is selected to recognize one alternative allele of an essential gene remaining in the cancer cell due to LOH in patients. . . therapy of cancer without suppression of the transplanted marrow. In an alternative embodiment, in an allogenic transplantation, therapy with an allele specific **inhibitor** that recognizes the one form of the essential gene that is present in cancer cells due to LOH in the recipient,. . . tissue for selective reimplantation. The present invention provides for an improved method for purging bone marrow of malignant cells using allele specific **inhibitors** of essential genes. The method involves identifying an essential gene with only one variant form remaining in the cancer cells due. . . The patient's bone marrow is then cultivated ex vivo using methods known in the art in the presence of an allele specific **inhibitor** that **inhibits** the allele that is present in the cancer cells, but not the alternative allele that is present in the heterozygous normal bone. . .

In another aspect, the invention provides a method for **inhibiting** growth of or killing a cell containing only one allelic form of a gene by contacting the cell with an **inhibitor** active on that allelic form. The gene has at least two sequence variants in a population, and belongs to one of the categories of essential genes described below. The **inhibitor** is less active on at least one other allelic form of the gene.

In preferred embodiments of the above aspects in which an allele specific **inhibitor** is used to **inhibit** a cell or to treat a patient, a plurality of different **inhibitors** may be used. Preferably different **inhibitors** target a plurality of different variances in a single target gene, or target variances in different target genes, or both. In particular embodiments a plurality of **inhibitors** is used simultaneously, in others there is serial administration using different **inhibitors** or different sets of

**inhibitors** in separate administrations, which may be performed as a single set of administrations in which each set of **inhibitors** is administered once, or in multiple serial administrations in which each set of **inhibitors** is

administered more than once. Such use of multiple **inhibitors** provides enhanced **inhibition**, which preferably includes killing, of the targeted cells. In addition, allele specific

**inhibitors** as described can be used in conjunction with other treatments for diseases and conditions, including in conjunction with other chemotherapeutic agents such. . .

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In a related aspect, an allele specific **inhibitor** can be used in conjunction with a conventional antiproliferative or chemotherapeutic agent or therapy, such therapies including radiation, immunotherapy, or surgery. In. . .

with the above aspects, in a further aspect the invention provides a pharmaceutical composition which includes at least one allele specific **inhibitor**.

In preferred embodiments the composition includes at least one allele specific

**inhibitor** and a pharmaceutically acceptable carrier. Such carriers are known in the art and some commonly used carriers are described in the Detailed Description

below. Also in preferred embodiments the composition includes two, three, or

more allele specific **inhibitors**, and may also include a pharmaceutically acceptable

carrier. In other preferred embodiments, the composition includes at least one

allele specific **inhibitor** and another antineoplastic agent, which need not be an

allele specific **inhibitor**. The embodiments of this aspect may also optionally

include diluents and /or other components as are commonly used in pharmaceutical compositions or formulations. In embodiments having a plurality

of allele specific **inhibitors**, the **inhibitors** may target a plurality of different

variances of a single target essential gene, or may target sequence variances of a plurality of. . .

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In accord with the use of pharmaceutical compositions, the present invention also provides a packaged pharmaceutical composition comprising an allele specific

**inhibitor** as described above, bearing a Food and Drug Administration use

indication for administration to a patient suffering from a cancer or.

Thus, similar to the above, the invention provides a method for identifying an

**inhibitor** potentially useful for treatment of cancer or other proliferative disorder.

The **inhibitor** is active on a conditionally essential gene, and

the gene is subject to loss of heterozygosity in a cancer. The method. . . least two alleles of a said gene which differ at at least one sequence variance site and testing a potential allele specific **inhibitor** to determine whether the potential **inhibitor** is active on at least one but less than all of the identified alleles. If the potential

**inhibitor inhibits** expression of at least one but less than all of the alleles or reduces the level of activity of a product of at least one but less than all of the alleles, this indicates that the potential allele specific **inhibitor** is, in fact such an allele-specific **inhibitor inhibitor**.

Similar to other types of target genes described above, the invention provides

**inhibitors**, methods for producing **inhibitors**, pharmaceutical compositions, methods for identifying potential patients, probes, and primers which target or recognize alleles of a conditionally essential gene or utilize **inhibitors** which target such genes.

. . . also provides methods for preventing the development of cancer, methods for treating a patient suffering from a cancer, and methods for **inhibiting** growth of a cells as described above except that the targeted cells are subjected to an altered condition such that the gene. . .

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In still another aspect, not requiring the use of allele specific **inhibitors**, but still utilizing information about sequence variance or allelic differences between normal somatic cells and cancer cells in a patient, the invention. . .

. . . above aspects, a conventional therapy acts on a protein or other molecular target in the same pathway as the allele specific **inhibitor**. As an example, the antineoplastic drug hydroxyurea, which **inhibits** ribonucleotide reductase (RR), can be used in conjunction with an allele specific **inhibitor** of RR subunit MI or M2 or another gene that encodes a product important in nucleotide synthesis. Similarly, the antiproliferative drug methotrexate **inhibits** the enzyme dihydrofolate reductase (DHFR), and can be used with allele specific **inhibitors** of DHFR that would result in a differential methotrexate effect on cancer tissues compared to normal proliferating tissues. Alternatively, methotrexate can be used with allele specific **inhibitors** of other genes important in folate metabolism to achieve an enhanced cancer cell specificity for methotrexate. Similarly, the anticancer drug 5-fluorouracil and related compounds can be administered together with an allele specific **inhibitor** of thymidylate synthase (TS)

in a patient heterozygous for TS and with LOH at the TS gene in proliferating cells, e.g., cancer cells. Alternatively, an allele specific **inhibitor** of 5-FU degradation or metabolism can be administered with 5-FU. For example, the enzyme dihydropyrimidine dehydrogenase, which catalyzes the first and rate. . .

LOH in one or more tumors or other proliferative disorders. Genes having these characteristics can then be used for identifying allele specific **inhibitors** and evaluated for use in the other methods of this invention. Such procedures are routine, as is shown by the Detailed Description. . .

In preferred embodiments of the above methods and **inhibitors** involving particular target genes or classes or categories of genes, the **inhibitor** or potential **inhibitor** is a ribozyme which is designed to specifically cleave a particular target allelic form of a gene (i.e., a nucleotide sequence such. . .

Similarly, in preferred embodiments the **inhibitor** or potential **inhibitor** is an oligonucleotide, e.g, an antisense oligonucleotide, preferably at least partially an oligodeoxyribonucleotide. The antisense oligonucleotide is complementary to a sequence which includes. . .

Thus, derivatives of nucleic acid **inhibitors** include modified nucleic acid molecules which may contain one or more of: one or more nucleotide analogs, including modifications in the sugar. . .

Similarly, in preferred embodiments the **inhibitor** or potential **inhibitor** is an antibody, preferably a monoclonal antibody, which may be complexed or conjugated with one or more other components, or a fragment. . .

An **inhibitor** may also be an oligopeptide or oligopeptide derivative. Such peptides may be natural or synthetic amino acid sequences, and may have modifications. . .

In other embodiments, the **inhibitor** is a small molecule, for example, a molecule of one of the structural types used for conventional anticancer chemotherapy.

region undergoes LOH at frequencies similar to the marker. Such gene identification thus further identifies particular cancers which can potentially be treated with **inhibitors** targeting sequence variances in those essential genes.

LOH for other such disorders and cancers, and can further readily identify essential genes which are potential targets for variance

specific **inhibition**

and the treatment of the corresponding condition and in other aspects of this invention.

72 hours after transfection with antisense oligonucleotides. Anti-ras is an oligonucleotide known to have antiproliferative effects against T24 cells. This oligonucleotide exhibits **inhibition** comparable to the anti-RPA70 oligonucleotide.

is two graphs showing that the proliferation of two cell lines homozygous for different variant forms of the RPA70 gene is **inhibited** to a greater degree by matched oligonucleotides than by oligomers having a single base mismatch. Cell proliferation was measured by BrdU incorporation.

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Fig. 13 is a graph showing **Inhibition** of BrdU incorporation in A549 cells by antisense oligonucleotides against the RPA 70 gene. Cells were transfected, as described previously, with a.

Fig. 20 is a graph showing **inhibition** of mutant ras using antisense oligonucleotides specific for the mutant form, based on information available in Schwab et al., 1994, PNAS 91:10460.

and the variant sequences within these genes, have utility for the therapy of cancer and other disorders through the discovery of variance-specific **inhibitors**.

Gene targets for a variance-specific **inhibition** strategy in this invention satisfy three criteria.

A large number of references have identified essential genes which constitute actual or potential targets for allele specific **inhibition**. The identification of essential genes can be approached in various ways.

carbohydrates, lipids, organic ions, and inorganic ions, or cytoskeletal elements. The loss of homeostasis often results in cell death or apoptosis or

**inhibition** of cell proliferation. Homeostasis in a living cell is dynamic, and programed changes in homeostasis are required through the life cycle.

those genes whose products are required for maintaining this homeostasis conducive to cell growth and survival are targets for anti-neoplastic e.g., anti-cancer, **inhibitors** as described in the methods herein. For example, many genes are involved in synthetic functions, allowing the cells to produce essential



cellular. . .

affecting the gene in a neoplastic disorder, establishes that the gene is a target gene potentially useful for identifying allele specific **inhibitors**

and for other aspects of the invention. In addition, as described, target genes are

useful in embodiments of certain aspects of the. . .

(Type I Beta) L25441

GGTI3 (Geranylgeranyltransferase) Y08201

Geranylgeranyltransferase (Type II Beta-Subunit) X98001

3.5 Genes required for regulation of levels of organic ions

Gdp Dissociation **Inhibitors**

GDI Alpha (RAB GDP Dissociation **Inhibitor** Alpha) D45021

Rab Gdp (RAB GDP Dissociation **Inhibitor** Alpha) D13988

4) Genes Required to Maintain Cellular Proteins at Levels Compatible with Cell Growth or Survival

Polypeptide precursor biosynthesis

Amino acid biosynthesis and. . . processing peptidase alpha subunit) D50913

MMP7 X07819

Proteasome Beta 6 D29012

Proteasome Beta 7 D38048

Proteasome C13 U 1 7496

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Proteasome C2 D00759

Proteasome C7-1 D26599

Proteasome **inhibitor** hPI31 subunit D88378

Proteasome P I 12 D44466

Proteasome P27 ABOO3177

Proteasome P55 ABOO3103

Ubiquitin System

Enzyme E2-17 Kd(Cyclin-selective ubiquitin carrier protein) U73379

ISOT-3(Ubiquitin carboxyl-terminal hydrolase. . .

Cell Shape and Motility at Levels

Compatible with Cell Growth or Survival

Cell structure genes (Cytoskeleton)

Actin X04098

Beta-Contractin X82207

Capping Protein Alpha U03851

CFL I (**Cofilin**, Non-Muscle Isoform) X95404

Desmin J03191

Dystrophin U26743

Gelsolin X04412

hOGG I (Myosin Light Chain Kinase) ABOO0410

IC Heavy Chain U31089

Itga2 (Integrin, Alpha 2 (CD49B, alpha. . .

Therapy with **inhibitors** of conditionally essential genes

involves administration of

the **inhibitor** together with a chemical or physical elements

that causes the target

gene to be essential for cell survival or proliferation. The use of allele specific

**inhibitors** in the current invention allows specific killing of cancer cells with such

chemical or physical agent since the gene function that is essential for the survival

of cells (in the presence of the chemical or physical agent) is

**inhibited** in the

cancer cell but not in the normal cell.

are responsible for maintaining cell survival or proliferation in the presence of a drug or biological material. For example, a drug that **inhibits** one pathway for maintaining the level of a cellular constituent within levels required for cell survival or proliferation may make alternative pathways essential. In a specific embodiment, the **inhibition** of a synthetic pathway for a cellular constituent may make alternative synthetic pathways essential for cell survival or proliferation. Alternatively, a . . . from the cell essential for continued survival or proliferation. It will be evident to those skilled in the art that anything which

**inhibits** the ability of a cell to survive in the presence of a specific drug that is designed to be cytostatic or cytotoxic, will sensitize that cell to the effects of the drug. A chemosensitizing agent is one that **inhibits** a function in the cell that is conditionally essential due to the administration of a chemotherapeutic drug.

in DNA repair may be essential that are not essential in the absence of the external physical force. An agent that **inhibits** functions in the cell that are essential due to the administration of ionizing radiation would be termed a radiosensitizing agent.

physical factors, determining whether such genes are subject to loss of heterozygosity, identifying alternative alleles in these genes and developing allele specific **inhibitors** of alternative forms of the gene.

The administration of such an **inhibitor** to a patient who has two alternative forms of the gene in normal cells but only one in the cancer cell. . .

Thiopurinemethyltransferase (GenBankU12387)  
e. Inactivation or transformation of other drugs including, but not limited to, purine analogs, folate analogs, topoisomerase **inhibitors** and tubulin acting drugs via specific enzymatic modification.

I-kappa B alpha (GenBank M69043)  
Increased expression of exogenous I kappa B-alpha, an **inhibitor** of NF-kappa B, increases cell sensitivity to ionizing radiation. Thus is conditionally essential for cells exposed to ionizing radiation.

affect the gene sequence, RNA sequence, or protein sequence of the gene or its gene products, which would facilitate the design of **inhibitors** of the protein product, or be a base difference anywhere within the genomic DNA sequence, including the promoter or intron

regions. Such DNA sequence variance can be exploited to design **inhibitors** of transcription or translation which distinguish between two allelic forms of the targeted gene. Sequence variants that do not alter protein sequence. .

. . .  
genes located in regions which are characteristically associated with LOH for a particular cancer, or other tumor are particularly advantageous targets for **inhibitors** useful for treatment of that cancer or tumor because such genes will also characteristically undergo LOH at high frequency. The fact that. . . LOH occurs before the clonal expansion of cancers in precancerous, abnormally proliferating tissue is potentially useful for preventing cancer with allele specific **inhibitors** of essential genes.

. . .  
disorder will indicate that the allele specific treatment would be appropriate for the disorder. For the application of the general allele specific **inhibition** strategy to such conditions (e.g.. selection of target gene and variance, identification of **inhibitors**, selection of composition and administration method appropriate for the condition and the **inhibitor**), the cells associated with the condition correspond with the tumor, e.g., cancer cells, for the 232/116 methods described in the Summary above.

. . .  
at least one marker. This does not necessarily represent the maximum fraction of plaques which could potentially be treated with allele specific **inhibitors** because the study did not attempt to determine the sites of maximum LOH on each arm. LOH which is partial arm. . .

. . .  
allele of the essential gene is lost from the patient's cancer cells, the retained allele can be targeted with an allele specific **inhibitor**. Such an **inhibitor** will kill, or reduce or prevent the growth of cancer cells by abolishing the function of an essential gene. Normal cells, which retain both uninhibited and **inhibited** alleles, will survive or grow due to the expression of the uninhibited allele. This is clearly indicated because tumor cells having only one allelic form (after LOH) thrive, thus, normal cells will also function normally with one of two allelic forms **inhibited**.

. . .  
neuroectodermal  
tumor  
Rhabdomyosarcoma  
17q Breast carcinoma  
Neurofibroma: N171  
22q Acoustic neurinoma  
1 8 Renal cell carcinoma Colorectal carcinoma

18q Breast carcinoma Ependymoma  
Colorectal carcinoma Meningioma  
Neurofibroma

V. Use of variance-specific **inhibitors** of essential genes to treat non-malignant, proliferative conditions.

will differ, with, for example, allele A of a hypothetical essential gene lost in some plaques and allele A' in others. An **inhibitor** of allele A would be expected to kill (or arrest growth of) only about half of all the plaques with allele. . . . plaques heterozygous for A. To kill the other half of the plaques with allele loss at the target locus would require an

**inhibitor** of A'. Simultaneous use of **inhibitors** of A and A' would be highly toxic to diploid normal cells. However serial use of an **inhibitor** directed to allele A followed by an **inhibitor** directed to A' (perhaps repeating treatment for several cycles, or even indefinitely) would alternately abolish essential gene function in one half of all haploid plaque cells and then the other half, leading eventually to death or sustained **inhibition** of proliferation of all plaque cells. Normal cells would retain

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50% gene function in the presence of **inhibitor** (either from allele A or allele A'). This therapeutic approach is applicable to the eradication of any clonal proliferation of cells in. . . .

surgically removed, LOH has been well described. As with atherosclerotic plaques, these tumors are frequently multifocal and therefore the approach of serial **inhibition** of allele A followed by

**inhibition** of allele A' would alternately abolish essential gene function in one half of all haploid tumor cells and then the other half, leading eventually to death or sustained **inhibition** of proliferation of all tumor cells.

one allelic form in individuals whose normal somatic cells are heterozygous for the particular essential gene. The essential gene can therefore be **inhibited** by an allele specific **inhibitor**, i.e., a variance specific **inhibitor**. In some conditions, however, multiple, independently arising lesions in an individual are subjected to LOH in a disease or condition, e.g., in. . . .

It was determined that such conditions can be treated using allele specific

**inhibitors** despite the presence of both alleles in cells related to the condition.

There are two strategies for such therapy. The first is to serially administer different **inhibitors** targeted to the different allelic forms of the target gene. This

can be accomplished by using **inhibitors** which target the alternative sequence variants of one sequence variance site. Simultaneous administration of **inhibitors** of both allelic forms of an essential gene would **inhibit** the cells which have undergone LOH at that gene, but would also **inhibit** the normal heterozygous cells of the individual. This treatment would **inhibit** essential functions in normal cells as well as cancer cells and have no advantage over the administration of conventional antiproliferative drugs, many of which are **inhibitors** of known essential functions. In contrast, administration of the first **inhibitor** targets the subset of cells which have only the first allelic form of an essential gene. As described for the general strategy, this **inhibitor** will not significantly affect the growth or survival of the normal heterozygous somatic cells. This first administration is followed by administration of a second **inhibitor**; the second

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**inhibitor** targets the cells which contain only the second allelic form of the gene, and again does not significantly affect the normal. . . will be useful. Similarly, recurring, or even indefinitely continued alternating administrations will provide useful treatment. Likewise, these methods can incorporate the use of **inhibitors** targeted to specific alleles of a plurality, e.g., 2, 3, 4, or more different target genes.

in non-malignant diseases are not clonal, there may be systematic loss of one parental chromosome allowing effective therapy with only one variance-specific **inhibitor**. This would occur, for example, if there were an inherited or early embryonic mutation within a tumor suppressor gene on one parental. . . of the corresponding normal tumor suppressor gene on the other parental chromosome would lead to abnormal proliferation. In such cases a variance-specific **inhibitor** of an essential gene that was closely linked to the normal tumor suppressor gene would preferentially kill cells in the proliferating lesion.

#### VI. Characteristics of allele-specific **inhibitors**

As indicated above allele specific **inhibitors** or allele specific anti-neoplastic agents represent a new approach to tumor therapy because they are lethal or significantly **inhibit** the growth only of tumor cells. The advantages of this approach include, first, lack of toxicity to the normal cells of. . . a therapeutic index greater than that of conventional tumor, e.g., cancer chemotherapy drugs, and second, it is not necessary that the **inhibitors** be targeted specifically to the tumor cells, as they can be administered

systemically. As also described above, usually an allele specific **inhibitor** is specific for a single

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sequence variance of an essential gene, though in some cases the **inhibitor** utilizes the joint effects of two or more sequence variances on a particular allele.

It is not necessary for the allele specific **inhibitor** to have absolute specificity.

of a gene product

encoded by the essential gene will often show a reduction in gene activity when

they take up the **inhibitors** of this invention, but should remain viable due to the

activity of the protein encoded by the uninhibited allele. On the other hand,

tumor cells expressing only one allele due to LOH, will respond to the **inhibitors**

of this invention which are specifically directed to the remaining allele, with a

greater reduction in gene activity. Growth of tumor cells exposed to the

**inhibitors** of this invention will be **inhibited** due to the suppression of either the synthesis or the biological activity of the essential gene product.

only two allelic forms in any given individual, the gene can have more than two allelic forms in a human population.

Accordingly,

**inhibitors** can be targeted to any of the alleles in the population. A particular

**inhibitor** will generally be targeted to a subset of the allelic forms; the members

of the subset will have a particular sequence variance which provides the specific

targeting. In some cases, however, the **inhibitor** will jointly target two, or

possibly more sequence variances.

Once two or more alleles are identified for a target essential gene, **inhibitors** of

high specificity for an allele can be designed or identified empirically. **Inhibitors**

that can be used in the present invention will depend on whether allelic variation

at a target locus affects the amino acid. . . the mRNA sequence, or the

DNA in intron and promoter regions. If there is variation at the protein level,

then classes of **inhibitors** would include low molecular weight drugs,

oligopeptides and their derivatives, and antibodies, including modified or partial

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antibody fragments or derivatives. For mRNA or DNA sequence variance the main class of **inhibitors** are complementary oligonucleotides

and their derivatives

and catalytic RNA molecules such as ribozymes, including modified ribozymes.

The generation of **inhibitors** of this invention can be

accomplished by a number of methods. The preferred method for the generation of specific **inhibitors** of the targeted allelic gene product uses computer modeling of both the target protein and the specific **inhibitor**. Other methods include screening compound libraries or microorganism broths, empirical screening of libraries of peptides displayed on bacteriophage, and various immunological approaches.

Further, in the treatment of cancer patients, a therapeutic strategy includes using more than one **inhibitor** of this invention to **inhibit** more than one target. In this manner, **inhibitors** directed to different proteins essential to cell growth can be targeted and **inhibited** simultaneously. The advantage of this approach is to increase the specificity of the **inhibition** of proliferation of cancer cells, while at the same time maintaining a low incidence of side effects.

structure of the alternate allelic forms of the proteins, determinants can be identified which distinguish the allelic forms. Novel low molecular weight

**inhibitors** or oligopeptides can then be designed for selective binding to these determinants and consequent allele-specific **inhibition**. Descriptions of targeted drug design can be found, for example, in I. Kuntz, Structure-Based Strategies for Drug Design and Discovery, Science 257:1078-1082. . . have been described in Piper et al., Studies Aided by Molecular Graphics of Effects of Structural Modifications on the Binding of Antifolate **Inhibitors** to Human Dihydrofolate Reductase, Proc Am. Assoc. Cancer Res. Annual Meeting 33:412 (1992); Hibert et al., Receptor 3D-Models and Drug Design, Therapie. . .

Low molecular weight **inhibitors** specific for each allelic protein form can be predicted by molecular modeling and synthesized by standard organic chemistry techniques. Computer modeling can. . .

The **inhibitors** of this invention can be identified by selecting those compounds that selectively **inhibit** the growth of cells expressing one allelic form of a gene, but do not **inhibit** the activity of the A allelic form.

#### B. Small Molecule **Inhibitors**

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Low molecular weight **inhibitors** can be identified and generated by at least one of the following methods; (1) screening of small organic molecules present in microorganism. . .

**Inhibition** of protein function following differential binding.

Several mechanisms of **inhibition** are possible including.

competitive **inhibition** of active sites or critical allosteric sites,  
allosteric **inhibition** of protein function,  
altering compartmentalization or stability, and  
**inhibition** of quaternary associations.

compounds that interact with particular features of a polypeptide or protein or protein complex, There are clear precedents for developing drugs, i.e., **inhibitors**, that are variance-specific including drugs that are allosteric **inhibitors** of protein functions. Several lines of experimental evidence demonstrate that small molecule variance specific  
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**inhibitors** can be designed and constructed for particular targets. Specifically.

Allosteric (noncompetitive) **inhibition** of protein function may be induced by binding ligands to many different surfaces of a protein. Ligands can cause allosteric **inhibition** by disturbing secondary, tertiary or quaternary (subunit-subunit) interactions of a protein. There is ample evidence that such effects can be induced by. . .

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Competitive **inhibitors** can exert variance-specific effects by exhibiting differential affinities for variant active sites, thereby interfering with binding of the substrate or critical allosteric. . .

Competitive **inhibitors** may bind with equal affinity for the active site but exerting different effects on the structure or function of the variant domain.

Allosteric **inhibitors** can exert variance-specific effects by binding differentially to variant forms of the active domain and distorting the structure or function of the. . .

model the topology and surface chemistry of the target in detail. These data are useful in optimizing the binding specificity or allosteric **inhibitory** function of the product through a series of iterative steps once a prototype binding ligand is identified. Structural modeling of the target. . .

Sites of allosteric **inhibition**  
Most drug development focuses on competitive **inhibitors** of protein action rather than noncompetitive, allosteric **inhibitors**. There is no a priori advantage to a competitive versus allosteric **inhibitor** except for the fact that medicinal chemistry



often begins with candidate molecules derived from natural substrates or cofactors. There are, in fact, conceptual advantages to allosteric **inhibitors** since each protein may contain multiple allosteric sites, and allosteric **inhibitors** may be effective at lower concentrations (e.g. those equivalent to the substrate) since there is no need to compete with the substrate. . .

Detailed crystallographic and other structural studies of a variety of enzymes show that the mechanism of allosteric **inhibition** commonly involves conformational changes (e.g. domain movements) far from the site of contact with the allosteric regulator. These data illustrate the cooperativity.

. . . several well-characterized proteins. Another is to examine the distribution of epitopes for antibodies that bind to the surface of a protein and

**inhibit** its function. Analyses of these types show that allosteric sites are widely dispersed within proteins and may comprise the majority of. . .

. . . Three HIV-1 RT structures have been published, including complexes with double stranded DNA at 3.0 A resolution and with the non-nucleoside **inhibitors** nevirapine (at 3.5A) and -APA (at 2.8A).

Two classes of HIV-1 RT **inhibitors** have been developed. The first class comprises nucleoside analogues including AZT, ddI and ddC. The second class comprises non-nucleoside analogues belonging to. . . 5 shows the location of selected mutations within HIV-1 RT that cause resistance to nucleoside analogues as well as the mechanism of

**inhibition** postulated from physical-chemical experiments and structural data; the list is not comprehensive.

Table 4  
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Location and postulated mechanism of amino acid substitutions which confer resistance to nucleoside analog **inhibitors**. trp266X - multiple substitutions.

. . . analog resistance arises from mutations in multiple domains. Many of the mutations are located far from the dNTP binding sites. These changes **inhibit** drug function by altering the conformation of the target protein in a manner analogous to those conformational changes that may be induced by an allosteric **inhibitor**.

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Table 5 summarizes the mutations that alter the function of non-nucleoside

**inhibitor** drugs

Table 5

Location and postulated mechanism of amino acid substitutions which

confer  
resistance to non-nucleoside analog **inhibitors**.

ala98gly 5b- 6 loop flexibility Pyridinone L-697661,  
Nevirapine  
leul.00ile 5b- 6 loop -branch Pyridinone L-697661  
Nevirapine, TIBO R82913  
lys101glu 5b- 6 loop charge Pyridinone. . . loop flexibility BHAP  
U-87201  
lys238thr 14 charge BHAP U-87201  
trp266X -thumb TIBO R82913  
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It is evident from these examples that the substitutions which  
**inhibit** drug functions  
are distributed across several domains. Different **inhibitory**  
mechanisms have been  
postulated in domains throughout the protein, based on the  
three-dimensional  
structure of the protein. Most involve conformational disruption of. .

Thyrotropin receptor Naturally occurring antibodies against the  
thyrotropin  
receptor can cause activation of thyroid function (Grave's disease) or  
**inhibition** of  
thyroid function (Hashimoto's disease). The sites within the thyrotropin  
receptor  
that are targeted by these natural antibodies have been mapped in detail  
and have  
been tested with monoclonal antibodies. Most of the **inhibitory**  
antibodies do not  
interfere with binding of thyrotropin to its receptor, and thus, are  
allosteric rather  
than competitive **inhibitors**. Several independent classes of  
**inhibitory** antibodies  
have been identified that bind to epitopes within different domains of  
the receptor.

can be deleted by site-directed mutagenesis without disrupting the  
function of the receptor. These experiments provide an explicit  
precedent for  
achieving allosteric **inhibitory** effects from ligands that  
target widely dispersed  
sequences within the protein.

Thermus aquaticus DNA polymerase The **inhibitory** activity of 24  
monoclonal  
antibodies to Thermus aquaticus DNA polymerase has been investigated.  
The  
antibodies recognized 13 non-overlapping epitopes. Antibody binding to  
eight  
epitopes was **inhibitory**. **Inhibitory** antibodies  
mapped to several distinct domains,  
including the 5'nuclease domain, the polymerase domain and the boundary  
region  
between the 5'nuclease and polymerase domains. Some antibodies  
recognized  
epitopes overlapping the DNA binding groove of the polymerase.  
Significantly, the  
**inhibitory** antibodies recognized epitopes constituting as much  
as 50% of the Taq  
polymerase surface, and the non-**inhibitory** antibodies a  
further -25%.

the pharmaceutical industry has worked to develop chemically modified penicillins and cephalosporins to elude inactivation by P-lactamases. In addition, a P-lactarnase **inhibitor** (clavulanic acid) has also been introduced into clinical use.

associated with drug resistance distributed evenly across the 740 amino acids of the protein. The mechanism by which some of these substitutions **inhibit** katG function can be inferred from the structure of the homologous yeast and E. coli enzymes and knowledge of the catalytic.

The application of small molecule **inhibitor** identification is specifically discussed in Example 39 below in connection with the methylguanine methyltransferase gene.

### C. Antibody **Inhibition**.

Antibody **inhibitors** are most effective when they are directed against cell surface proteins or receptors. If the essential protein produced by the targeted allele is not a cell surface protein or receptor, the development of antibody **inhibitors** may also require the use of a special antibody-delivery system to facilitate entry of the antibody into the tumor cells. The plasma. . . the structure of the variable region of allele specific antibodies can be used as the basis for design of smaller allele specific **inhibitory** molecules.

receptors or other polypeptides essential for cell viability. Methods for screening peptide sequences which have high specificity for binding to, and functional **inhibition** of, a specific polypeptide target have been well described previously. Scott, J.K. and Smith G.P., Searching for Peptide Ligands with an Epitope. . . by phage display of polypeptide sequences as well as direct screening of peptides or mixtures of synthetic peptides for binding to or **inhibition** of the target Rinctional polypeptide.

### Ribozymes

Oligonucleotides or oligonucleotide analogs which interact with complementary sequences of cellular target DNA or RNA can be synthesized and used to **inhibit** or control gene expression at the levels of transcription or translation. The oligonucleotides of this invention can be either oligodeoxyribonucleotides or oligoribonucleotides, or. . . they can act enzymatically, such as ribozymes. Both antisense RNA and DNA can be used in this capacity as chemotherapeutic agents for **inhibiting** gene transcription or translation. Trojan, J.,

et al, Treatment and prevention of rat glioblastoma, by immunogenic C6 cells expressing antisense insulin-like growth. . .

**Inhibitory** complementary oligonucleotides may be used as **inhibitors** for cancer therapeutics because of their high specificity and lack of toxicity.

Included in the scope of the invention are oligoribonucleotides, including antisense RNA and DNA molecules and ribozymes that function to **inhibit** expression of an essential gene in an allele specific manner. Anti-sense RNA and DNA molecules act to directly block the translation of. . .

A specific application of generating **inhibitors** which are either complementary oligonucleotides or **inhibitory** oligopeptides is described in Holzmayer, Pestov, and Roninson, Isolation of dominant negative mutants and **inhibitory** antisense RNA sequences by expression selection of random DNA fragments, Nucleic Acids Research 20:711-717 (1992). In this study, genetic suppressor elements (GSEs). . .

Preferred oligonucleotide **inhibitors** include oligonucleotide analogues which are resistant to degradation or hydrolysis by nucleases. These analogues include neutral, or nonionic, methylphosphonate analogues, which retain. . .

F, Gene Therapy  
Nucleic acid molecules encoding oligonucleotide or polypeptide **inhibitors** will also be useful in gene therapy (reviewed in Miller, Nature 357:455-460, (1992). Miller indicates that advances have resulted in practical approaches. . .

A nucleic acid sequence encoding an **inhibitor** may be administered utilizing an ex vivo approach whereby cells are removed from an animal, transduced with the nucleic acid sequence and reimplanted. . .

Many nonviral techniques for the delivery of a nucleic acid sequence encoding an

**inhibitor** into a cell can be used, including direct naked DNA uptake (e.g., Wolff et al., Science 247: 1465-1468, 1990), receptor-mediated DNA. . .

its simplest form, gene transfer can be performed by simply injecting minute amounts of DNA (e.g., a plasmid vector encoding an **inhibitor**) into the nucleus of a cell, through a process of microinjection. Capecchi MR, Cell 22:479-88 (1980).

232/116

In another preferred embodiment, a vector having nucleic acid sequences encoding an allele specific **inhibitor** is provided in which the nucleic

acid sequence is  
expressed only in specific tissue. Examples or methods of achieving  
tissue-specific  
gene expression. . .

V11. Utility of allele-specific **inhibitors** of essential genes  
A, Conditions susceptible to therapy.

The fraction of all cancers could be treated with allele specific  
**inhibitors** directed  
against allele specific essential gene targets is a function of the  
frequency of the  
target allele and the frequency of LOH.. . . exist in two allelic  
forms, each with an allele  
frequency of 0.5 so that half the population would be heterozygous. An  
**inhibitor** of  
one allele of such an ideal target would be a useful agent for 25% of  
all cancer  
patients. An **inhibitor** of the other allele of the same ideal  
target would be  
therapeutic for an additional 25% of all patients, making 50%. . .

Allele specific **inhibitors** of both alleles of such targets  
would be expected to  
address  $0.4 \times 0.5 = 0.2$  or 20% of the relevant. . .

<-----User Break----->

```
=> s actin
      15854 ACTIN
      208 ACTINS
L24    15915 ACTIN
      (ACTIN OR ACTINS)

=> s stabil?
L25    282338 STABIL?

=> s ewing?
L26    3185 EWING?

=> s 126 and 124
L27    1098 L26 AND L24

=> s 127 and 125
L28    1004 L27 AND L25

=> s 124/ab
      151 ACTIN/AB
      1 ACTINS/AB
L29    152 (ACTIN/AB)
      ((ACTIN OR ACTINS)/AB)

=> s 129 and 126
L30    5 L29 AND L26

=> s 130 and 125
L31    5 L30 AND L25

=> d ibib 1-5
```

```
L31    ANSWER 1 OF 5      PCTFULL    COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:      2006029046 PCTFULL    ED 20060403    EW 200611
TITLE (ENGLISH):      USE OF LEPTIN IN WOUND HEALING
```

TITLE (FRENCH): UTILISATION DE LEPTINE DANS LA GUERISON DE PLAIE  
 INVENTOR(S): SIERRA-HONIGMANN, Maria Rocio, 656 Camino de la Luna,  
 Thousand Oaks, California 91320, US  
 PATENT ASSIGNEE(S): YALE UNIVERSITY, Office of Cooperative Research, 433  
 Temple Street, New Haven, Connecticut 06511, US  
 AGENT: LEVY, Seth, D. et al.\$, Suite 2400, 865 South Figueroa  
 Street, Los Angeles, California 90017-2566;  
 90017-2566\$, US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2006029046	A2	20060316

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
 CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
 HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU  
 LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL  
 PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA  
 UG US UZ VC VN YU ZA ZM ZW

RW (ARIPO):

BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT  
 LT LU LV MC NL PL PT RO SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2005-US31455 A 20050902

PRIORITY INFO.:

US 2004-60607115 20040903

L31 ANSWER 2 OF 5

ACCESSION NUMBER:

PCTFULL COPYRIGHT 2006 Univentio on STN  
 2005042726 PCTFULL ED 20050519 EW 200519

TITLE (ENGLISH):

METHODS FOR MODULATING AN IMMUNE RESPONSE BY MODULATING  
 KRC ACTIVITY

TITLE (FRENCH):

METHODES PERMETTANT DE MODULER UNE REPOSE IMMUNITAIRE  
 PAR MODULATION DE L'ACTIVITE DE KRC

INVENTOR(S):

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 02146, US [US, US]

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AGENT:

DECONTI, Giulio, A.\$, Lahive & Cockfield, LLP, 28 State  
 Street, Boston, MA 02109\$, US

LANGUAGE OF FILING:

English

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005042726	A2	20050512

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
 CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
 HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV  
 MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO  
 RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ  
 VC VN YU ZA ZM ZW

RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW  
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT  
LU MC NL PL PT RO SE SI SK TR  
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
APPLICATION INFO.: WO 2004-US36641 A 20041103  
PRIORITY INFO.: US 2003-10/701,401 20031103

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2003027235 PCTFULL ED 20030410 EW 200314  
TITLE (ENGLISH): AFAP SEQUENCES, POLYPEPTIDES, ANTIBODIES AND METHODS  
TITLE (FRENCH): SEQUENCES AFAP, POLYPEPTIDES, ANTICORPS ET PROCEDES  
ASSOCIES  
INVENTOR(S): FLYNN, Daniel, C., 418 Shawnee Drive, Morgantown, WV  
26508-0911, US  
PATENT ASSIGNEE(S): WEST VIRGINIA UNIVERSITY RESEARCH CORPORATION, P.O. Box  
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LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003027235	A2	20030403

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI  
SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW  
GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
AM AZ BY KG KZ MD RU TJ TM  
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC  
NL PT SE SK TR

RW (ARIPO): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
RW (EAPO):  
RW (EPO):  
RW (OAPI):  
APPLICATION INFO.: WO 2002-US29559 A 20020918  
PRIORITY INFO.: US 2001-60/323,866 20010921

L31 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2002102846 PCTFULL ED 20030115 EW 200252  
TITLE (ENGLISH): PHARMACEUTICAL COMPOSITION FOR DIAGNOSIS, PREVENTION OR  
TREATMENT OF A TUMOROUS STATE, COMPRISING A MODULATOR  
OF THE ACTIN POLYMERISATION STATE  
TITLE (FRENCH): COMPOSITION PHARMACEUTIQUE POUR LE DIAGNOSTIC, LA  
PREVENTION OU LE TRAITEMENT D'UNE PATHOLOGIE TUMORALE,  
COMPRENANT UN AGENT MODULATEUR DE L'ETAT DE  
POLYMERISATION DE L'ACTINE  
INVENTOR(S): AUCLAIR, Christian, 22, avenue Parmentier, F-75011  
Paris, FR [FR, FR];  
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 HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013  
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 SUBRA, Frederic, 3 bis, rue d'Athenes, F-75009 Paris,  
 FR [FR, FR], for US only  
 AGENT: BRESSE, Pierre\$, Bresse-Majerowicz, 3, avenue de  
 l'Opera, F-75001 Paris\$, FR  
 LANGUAGE OF FILING: French  
 LANGUAGE OF PUBL.: French  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

	NUMBER	KIND	DATE
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	WO 2002102846	A2	20021227
DESIGNATED STATES			
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW		
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW		
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM		
RW (EPO):	AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR		
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2002-FR2106	A	20020618
PRIORITY INFO.:	FR 2001-01/07976		20010618

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 1999022028 PCTFULL ED 20020515  
 TITLE (ENGLISH): MODULATORS OF ACTIN  
 TITLE (FRENCH): MODULATEURS D'ACTINE  
 INVENTOR(S): KING, Mary-Claire;  
 LYNCH, Eric, D.;  
 LEE, Ming, K.;  
 MORROW, Jan, E.;  
 WELCSH, Piri, L.;  
 LEON, Pedro, E.  
 PATENT ASSIGNEE(S): THE UNIVERSITY OF WASHINGTON;  
 THE UNIVERSITY OF COSTA RICA  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

	NUMBER	KIND	DATE
	-----		
	WO 9922028	A1	19990506
DESIGNATED STATES			
W:	CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE		
APPLICATION INFO.:	WO 1998-US23024	A	19981029
PRIORITY INFO.:	US 1997-60/063,737		19971029
	US 1998-09/080,897		19980518



=> d kwic 31

5 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE  
The answer numbers requested are not in the answer set.

ENTER ANSWER NUMBER OR RANGE (1):eng

ANSWER NUMBERS NOT CORRECTLY SPECIFIED

Enter an answer number, Example: 10  
several answer numbers, Example: 3,7,10  
a range of answer numbers, Example: 5-10  
or a combination of these. Example: 3,7,9-10,15  
ENTER ANSWER NUMBER OR RANGE (1):end

=> d kwic 3

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ABEN The present invention comprises reagents and methods which target  
**actin** filaments or the cellular signals that control  
**actin** filament integrity. Specifically, the invention provides  
novel **actin** binding polypeptides (e.g., human AFAP  
polypeptides), antibodies which specifically recognize the same, nucleic  
acids encoding the same, and methods for. . .

DETD . . . aspect, the pathology is cancer, e.g., such as breast cancer,  
colon cancer,  
prostate cancer, lung cancer, a cancer involving neural cells,  
**Ewing** sarcoma and  
rhabdomyosarcoma.

. . .  
acids comprising one or more of modified bases, sugars, and  
intermicleotide linkages  
which preferably have the substantially the same or enhanced  
**stability** and/or specificity for a  
target nucleic acid as the nucleic acids from which they are derived.

. . .  
Antisense nucleic acids can also be  
chemically synthesized and can be deoxynucleotides or modified forms  
thereof which are  
selected to have enhanced **stability** in vivo.

. . .  
activated in a number of human cancers including breast cancer,  
colon cancer, prostate cancer, lung cancer (e.g., small lung cell  
carcinoma), neuroblastoma,  
**Ewing** sarcoma and rhabdomyosarcoma (Cartwright et al., 1990,  
supra; Rosen et al., 1986,  
supra).

. . .  
breast cancer, colon cancer, prostate cancer, lung cancer  
(e.g., small lung cell carcinoma), a cancer involving neural cells  
(e.g., such as neuroblastoma),  
**Ewing** sarcoma and rhabdomyosarcoma.

. . .  
forms thereof. In one aspect, the condition is cancer (e.g.,  
such as breast cancer, colon cancer, prostate cancer, lung cancer,  
neuroblastoma, **Ewing** sarcoma  
and rhabdomyosarcoma). In another aspect, the condition is a  
neurological disease (which can

47

The agents, agonists, and antagonists may be formulated. . .

. . .  
and coverslips and observed under confocal microscopy (Zeiss,  
Oberkochen, Germany). Samples for negative staining were adsorbed to  
grids coated with  
nitrocellulose and **stabilized** with carbon (Ernest F. Fullam,

Latham, NY). Unbound protein was removed by successive washes with buffer and water before staining with.  
.

CLMEN. . . said cancer is selected from the group consisting of. breast cancer, colon cancer, prostate cancer, lung cancer, a cancer involving neural cells, **Ewing** sarcoma and rhabdomyosarcoma.

=> d kwic 5

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
ABEN The invention provides methods and compositions which find use, i(inter alia), for modulating the **stabilization** of **actin** filaments. The compositions may comprise one or more polypeptide moieties derived from a novel human diaphanous polypeptide and/or one or. . .  
ABFR L'invention concerne des procedes et des compositions permettant, entre autres choses, de moduler la **stabilisation** des filaments d'actine. Ces compositions peuvent comprendre une ou plusieurs fractions de polypeptide derivees d'un nouveau polypeptide diaphane de l'homme. . .

DETD INTRODUCTION  
Field of the Invention  
The invention relates to a class of polypeptides involved in actin **stabilization**.  
. . .  
of the Invention  
The actin cytoskeleton plays a central role in defining cellular structure and effecting dynamic changes in morphology. By selectively **stabilizing** and destabilizing actin polymerization, the cell is able to effect a wide range of structural reorganization and effect phenomena such as cell. . .  
  
the progress of many pathogenic infections, invasion and metastasis of neoplasia, fertilization, clotting and wound repair, etc., the **stability** of actin polymerization is a choice target for therapeutic intervention. In fact, potent drugs effecting actin filament destabilization and **stabilization** such as fungal-derived alkaloids including the cytochalasins and phalloidins are well known. Here we disclose a new family of modulators of actin polymer **stabilization** derived from a novel human diaphanous protein and gene.

SUMMARY OF THE INVENTION  
The invention provides methods and compositions which find use. inter alia, for modulating the **stabilization** of actin filaments. The compositions may comprise one or more polypeptide moieties derived from a novel human diaphanous polypeptide and/or one. . .

. . .  
other polypeptide moieties, complexed in a wide variety of covalent and/or non-covalent associations and binding complexes, etc., which may provide enhanced activity, **stability**, availability, targeting, etc.

polypeptide  
hDial-del-15: CYCLIN B2 - residues 1141-1171 of SEQ ID NO:2 fusion  
polypeptide  
The invention provides methods and compositions of selectively  
modulating  
cytoskeletal de/**stabilization** and/or the effective  
concentration of a human diaphanous protein  
within a target cell. The general methods involve introducing into the  
target. . . the human diaphanous polypeptide moiety, the modulator  
may  
comprise a wide variety of additional moieties, including moieties which  
provide for  
detection, targeting, **stability**, proteolytic resistance, etc.  
Preferred modulators demonstrate  
cytoskeletal de/**stabilization** with several alternative methods  
of introduction, including direct  
medium uptake, uptake facilitated by chaotropic agents including  
detergents (e.g. TWEEN20,  
etc.), guanadine salts, . . .

to a probe specific for the binding agent. Agents of  
particular interest modulate human diaphanous polypeptide function, e.g.  
human diaphanous

5  
polypeptide-dependent actin de/**stabilization**.

usually RNA or DNA, it is often advantageous to use nucleic acids  
comprising other bases or nucleotide analogs to provide modified  
**stability**, etc.

3.0 were transferred to a UNIX-based Sun workstation for cont-ig'  
assembly and blast analysis. The computer program PHRED (Green P and  
Ewing B. 1996.

phrap.docs/ phred.html) was used to assign bases  
to the electropherograms. After eliminating vector sequences, the  
program PHRAP (Green P  
10 and Ewing B. 1996. [http://www.bozeman.mbt.washington.edu/  
phrap.docs/ phrap.html](http://www.bozeman.mbt.washington.edu/phrap.docs/phrap.html)) was  
used to analyze the sequences, identify overlapping individual  
sequences, and assemble them  
into contigs. To. . .

daily blood and peritoneal sample to evaluate peritoneal fluid cell  
counts,  
hematological cell counts, serum chemistries, bacterial cultures as  
needed, vector **stability**,  
viral uptake by cells, expression of hDial gene and presence of  
antibodies to vector envelope  
proteins. At four week intervals patients are. . .

Detection of vector **stability** and expression. DNA is prepared  
from cell samples by  
hypotonic lysis, digestion with proteinase K (Boehringer Mannheim,  
Indianapolis. Indiana)  
and SDS, followed. . .

PCR primers specific for the neo sequences within the LXSN-hDialsv  
vector are  
employed for determination of vector presence and **stability**  
within patient samples. RT-PCR  
is performed by our published methods (Thompson, M. E., et al. Nature

Genetics 9, 444-  
450] 1995.).

=> s ewing sarcoma or (ewing? sarcoma  
UNMATCHED LEFT PARENTHESIS 'OR (EWING?'

The number of right parentheses in a query must be equal to the  
number of left parentheses.

=> s ewing sarcoma or (ewing? sarcoma)  
3035 EWING  
132 EWINGS  
3112 EWING  
      (EWING OR EWINGS)  
18118 SARCOMA  
5088 SARCOMAS  
5 SARCOMATA  
19804 SARCOMA  
      (SARCOMA OR SARCOMAS OR SARCOMATA)  
392 EWING SARCOMA  
      (EWING (W) SARCOMA)  
3185 EWING?  
18118 SARCOMA  
5088 SARCOMAS  
5 SARCOMATA  
19804 SARCOMA  
      (SARCOMA OR SARCOMAS OR SARCOMATA)  
400 EWING? SARCOMA  
      (EWING? (W) SARCOMA)  
L32 400 EWING SARCOMA OR (EWING? SARCOMA)

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006  
E "DOLASTATIN"/CN 25

L1 1 S E6

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006

L2 52669 S ACTIN  
L3 812 S COFILIN  
L4 1968300 S ANTAG? OR INHIBIT?  
L5 222 S L4 (L) L3  
L6 1659 S EWING?  
L7 1 S L6 AND L5  
L8 22 S L1  
L9 0 S L8 AND L6  
L10 224 S ZYXIN  
L11 3 S L10 AND L6  
L12 6 S L3 AND L6  
L13 4 S L12 AND L4  
L14 989 S PHOSPHOINOSITOL?  
L15 0 S L14 AND L6  
L16 98 S PHOSPHOTIDYLINOSITOL  
L17 0 S L15 AND L6

FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006

L18 188 S COFILIN  
L19 3185 S EWING?  
L20 19 S L19 AND L18  
L21 198141 S ANTAG? OR INHIBIT?  
L22 19 S L20 AND L21

L23 4 S L22 NOT PY>2001  
 L24 15915 S ACTIN  
 L25 282338 S STABIL?  
 L26 3185 S EWING?  
 L27 1098 S L26 AND L24  
 L28 1004 S L27 AND L25  
 L29 152 S L24/AB  
 L30 5 S L29 AND L26  
 L31 5 S L30 AND L25  
 L32 400 S EWING SARCOMA OR (EWING? SARCOMA)

=> s 132 and 124

L33 165 L32 AND L24

=> s 133 and 125

L34 137 L33 AND L25

=> s 134 not py>2001

488865 PY>2001

L35 54 L34 NOT PY>2001

=> s 135 and 129

L36 0 L35 AND L29

=> s 124/clm

L37 1198 (ACTIN/CLM)

=> s 137 and 135

L38 5 L37 AND L35

=> s 124/ti

L39 44 (ACTIN/TI)

=> s 139 and 135

L40 0 L39 AND L35

=> d ibib 138 1-5

L38 ANSWER 1 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 2001055368 PCTFULL ED 20020827  
 TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES  
 TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS  
 INVENTOR(S): ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;  
 ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055368	A1	20010802

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
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APPLICATION INFO.:  
PRIORITY INFO.:

WO 2001-US1348	A 20010117
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US 2001-60/259,678	20010105

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 2001055328 PCTFULL ED 20020827  
 TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES  
 TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS  
 INVENTOR(S): ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;  
 ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055328	A2	20010802

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APPLICATION INFO.:  
 PRIORITY INFO.:

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US 2001-60/259,678	20010105

L38	ANSWER 3 OF 5	PCTFULL	COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:		2001055201	PCTFULL ED 20020827
TITLE (ENGLISH):		NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES	
TITLE (FRENCH):		ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS	
INVENTOR(S):		ROSEN, Craig, A.;	
		BARASH, Steven, C.;	
		RUBEN, Steven, M.	
PATENT ASSIGNEE(S):		HUMAN GENOME SCIENCES, INC.;	
		ROSEN, Craig, A.;	
		BARASH, Steven, C.;	
		RUBEN, Steven, M.	
DOCUMENT TYPE:		Patent	
PATENT INFORMATION:		NUMBER	KIND DATE

## DESIGNATED STATES

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## APPLICATION INFO.:

## PRIORITY INFO.:

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WO 2001055201

A1 20010802

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SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
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WO 2001-US1317 A 20010117

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US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 2001054733 PCTFULL ED 20020827  
 TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES  
 TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS  
 INVENTOR(S): ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;  
 ROSEN, Craig, A.;  
 BARASH, Steven, C.;  
 RUBEN, Steven, M.  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001054733	A1	20010802

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 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
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APPLICATION INFO.:  
 PRIORITY INFO.:

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US 2000-60/232,399	20000914
US 2000-60/232,400	20000914
US 2000-60/232,397	20000914
US 2000-60/233,063	20000914
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US 2000-60/233,065	20000914
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US 2000-60/234,223	20000921
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US 2000-60/234,997	20000925
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US 2000-60/235,484	20000926
US 2000-60/235,834	20000927
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US 2000-60/236,369	20000929
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US 2000-60/236,370	20000929
US 2000-60/236,368	20000929
US 2000-60/236,367	20000929
US 2000-60/237,039	20001002
US 2000-60/237,038	20001002
US 2000-60/237,040	20001002
US 2000-60/237,037	20001002
US 2000-60/236,802	20001002

US 2000-60/239,937	20001013
US 2000-60/239,935	20001013
US 2000-60/241,785	20001020
US 2000-60/241,809	20001020
US 2000-60/240,960	20001020
US 2000-60/241,787	20001020
US 2000-60/241,808	20001020
US 2000-60/241,221	20001020
US 2000-60/241,786	20001020
US 2000-60/241,826	20001020
US 2000-60/244,617	20001101
US 2000-60/246,474	20001108
US 2000-60/246,532	20001108
US 2000-60/246,476	20001108
US 2000-60/246,526	20001108
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US 2000-60/249,300	20001117
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US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 5 OF 5  
 ACCESSION NUMBER:  
 TITLE (ENGLISH):

PCTFULL COPYRIGHT 2006 Univentio on STN  
 2001053514 PCTFULL ED 20020827  
 TOXICANT-INDUCED DIFFERENTIAL GENE EXPRESSION

TITLE (FRENCH): EXPRESSION GENETIQUE DIFFERENTIELLE INDUITE PAR  
SUBSTANCES TOXIQUES  
INVENTOR(S): REIDHAAR-OLSON, John, F.  
PATENT ASSIGNEE(S): GLAXO GROUP LIMITED;  
REIDHAAR-OLSON, John, F.  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 2001053514	A1	20010726

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE  
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE  
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX  
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA  
UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG  
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI  
FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA  
GN GW ML MR NE SN TD TG

APPLICATION INFO.:  
PRIORITY INFO.:

WO 2001-US1920	A	20010119
US 2000-09/489,220		20000121



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NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
NEWS	9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist \$500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006

=> file pctfull

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006

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FILE LAST UPDATED: 11 APR 2006 <20060411/UP>

MOST RECENT UPDATE WEEK: 200614 <200614/EW>

FILE COVERS 1978 TO DATE

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SEE

<http://www.stn-international.de/stndatabases/details/ipc-reform.html> >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE

(last updated April 10, 2006) <<<

=> s jasplakinolide

171 JASPLAKINOLIDE

1 JASPLAKINOLIDES

L1 171 JASPLAKINOLIDE

(JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s ewing? (2W) sarcoma

3185 EWING?

18118 SARCOMA

5088 SARCOMAS

5 SARCOMATA

19804 SARCOMA

(SARCOMA OR SARCOMAS OR SARCOMATA)

L2 1574 EWING? (2W) SARCOMA

=> s 12 and 11

L3 36 L2 AND L1

=> s 13 not py>2001

488865 PY>2001

L4 1 L3 NOT PY>2001

=> d ibib

L4 ANSWER 1 OF 1

ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH):

INVENTOR(S):

PATENT ASSIGNEE(S):

LANGUAGE OF PUBL.:

PCTFULL COPYRIGHT 2006 Univentio on STN

2000071135 PCTFULL ED 20020515

ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS

AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE

BOROPROLINE

WALLNER, Barbara, P.;

MILLER, Glenn

POINT THERAPEUTICS, INC.

English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000071135	A1	20001130

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ  
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN  
MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ  
TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK  
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM  
GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2000-US14505 A 20000525

PRIORITY INFO.:

US 1999-60/135,861 19990525

=> d kwic

L4 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . myxoid liposarcomas and pleiomorphic  
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral  
nerve sheath  
tumors (also called malignant schwannomas, neurofibrosarcomas, or  
neurogenic sarcomas),  
Ewing's tumors (including Ewing's sarcoma of bone,  
extraskkeletal [not bone] Ewing's  
io sarcoma, and primitive neuroectoderinal tumor [PNET]),  
synovial sarcoma, angiosarconias,  
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,  
hemangioendothelioma,  
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),  
dermatofibrosarcoma  
protuberans (DFSP),. . .

immunostimulant peptides-, insulin-like growth factor-I receptor  
inhibitoi, interferon  
agonists; interferons; interleukins; iobenguane; lododoxorubicin;  
lporneanol, 4-; irinotecan;  
iropact; irsogladine; isobengazole; isohomohalicondrin B; itasetron;  
jasplakinolide;  
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;  
lenograstim; lentinan sulfate;  
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha  
interferon; leuprolide +  
estrogen + progesterone; leuprorelin;. . .

=> s hepatocarcinoma? or mesenchymal or neuroectodermal

463 HEPATOCARCINOMA?

4765 MESENCHYMAL

1 MESENCHYMALS

4765 MESENCHYMAL

(MESENCHYMAL OR MESENCHYMALS)

922 NEUROECTODERMAL

1 NEUROECTODERMALS

922 NEUROECTODERMAL

(NEUROECTODERMAL OR NEUROECTODERMALS)

L5 5608 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s 15 and 14

L6

1 L5 AND L4

=> d kwic\  
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The following are valid formats:

ALL, MAX-----BIB plus IND plus ABS plus TX  
ALLG-----ALL, MAX plus GI  
BIB-----AN, ED, UP, EW, UW, TIEN, TIFR, TIDE, TIES, IN, PA, LA, LAF  
DT, PI, DS, AI, PRAI  
BIBG-----BIB plus GI  
IND, IPC-----ICM, ICS  
ABS-----ABEN, ABF, ABFR, ABDE, ABES  
TX-----DETD, CLM  
IALL,IMAX-----ALL indented with text labels  
IALLG,IMAXG-----IALL, IMAX plus GI  
DALL-----Delimited ALL format  
STD-----BIB plus IND  
STDG-----STD plus GI  
ISTD-----STD indented with text labels  
ISTDG-----ISTD plus GI  
BRIEF-----BIB plus ABS  
BRIEFG-----BIB plus ABS plus GI  
IBRIEF-----BRIEF indented with text labels  
IBRIEFG-----IBRIEF plus GI  
SCAN-----TI (random display without AN)  
TRIAL (TRI)-----FA, TI, CLMN, DETN  
SAMPLE (SAM)-----FA, TI, CLMN, DETN  
FREE-----FA, TI, CLMN, DETN  
ENTER DISPLAY FORMAT (STD):kwic

L6 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . epithelium eductus semicircularis, enamel epithelium, false  
epithelium,  
germinal epithelium, gingival epithelium, glandular epithelium,  
glomerular epithelium,  
laminated epithelium, epithelium of lens, epithelium lentis,  
**mesenchymal** epithelium,  
olfactory epithelium, pavement epithelium, pigmentary epithelium,  
pigmented epithelium,  
protective epithelium, pseudostratified epithelium, pyramidal  
epithelium, respiratory  
epithelium, rod epithelium, serniniferous epithelium, sense epithelium,.  
. . .  
gelatinous carcinoma, giant cell  
carcinoma, gigantocellulare, glandular carcinoma, granulosa. cell  
carcinoma, hair-matrix  
carcinoma, hematoid carcinoma, hepatocellular carcinoma (also called  
hepatoma, malignant  
hepatoma and **hepatocarcinoma**), Mirthle cell carcinoma, hyaline  
carcinoma, hypernephroid  
carcinoma, infantile embryonal carcinoma, carcinoma in situ,  
intraepidermal carcinoma,  
intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-cell  
carcinoma, lenticular  
carcinoma,. . .  
. . .  
characterized by an abnormal mammalian cell proliferation to be  
treated by the methods of the invention include sarcomas. Sarcomas are  
rare **mesenchymal**

neoplasms that arise in bone and soft tissues. Different types of sarcomas are recognized and these include: liposarcomas (including myxoid liposarcomas and pleiomorphic liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral nerve sheath tumors (also called malignant schwannomas, neurofibrosarcomas, or neurogenic sarcomas), Ewing's tumors (including Ewing's sarcoma of bone, extraskeletal [not bone] Ewing's sarcoma, and primitive neuroectodermal tumor [PNET]), synovial sarcoma, angiosarcomas, hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma, hemangioendothelioma, fibrosarcoma, desmoid tumor (also called aggressive fibromatosis), dermatofibrosarcoma protuberans (DFSP),. . .

immunostimulant peptides-, insulin-like growth factor-I receptor inhibitor, interferon agonists; interferons; interleukins; iobenguane; lododoxorubicin; lporneanol, 4-; irinotecan; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone; leuprorelin;. . .

=> d his

(FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006

L1 171 S JASPLAKINOLIDE  
L2 1574 S EWING? (2W) SARCOMA  
L3 36 S L2 AND L1  
L4 1 S L3 NOT PY>2001  
L5 5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL  
L6 1 S L5 AND L4

=> s 15 and 11

L7 37 L5 AND L1

=> s 17 not py>2001

488865 PY>2001

L8 4 L7 NOT PY>2001

=> d ibib 1-4

L8 ANSWER 1 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2001089520 PCTFULL ED 20020826  
TITLE (ENGLISH): DEHYDROASCORBIC ACID FORMULATIONS AND USES THEREOF  
TITLE (FRENCH): FORMULATIONS D'ACIDE DEHYDROASCRBIQUE ET LEURS UTILISATIONS  
INVENTOR(S): OLSON, William, C.;  
ISRAEL, Robert, J.;  
BOYD, Thomas, A.  
PATENT ASSIGNEE(S): PROGENICS PHARMACEUTICALS, INC.;  
OLSON, William, C.;  
ISRAEL, Robert, J.;

DOCUMENT TYPE:  
PATENT INFORMATION:

BOYD, Thomas, A.  
Patent

NUMBER                    KIND            DATE

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WO 2001089520                A2 20011129

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG  
CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2000-US41407                A 20001020

PRIORITY INFO.:

US 2000-60/205,870                20000519

L8 ANSWER 2 OF 4

PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER:

2001029235 PCTFULL ED 20020820

TITLE (ENGLISH):

TMS1 COMPOSITIONS AND METHODS OF USE

TITLE (FRENCH):

COMPOSITIONS DU GENE TMS1 ET PROCEDES D'UTILISATION

INVENTOR(S):

VERTINO, Paula, M.

PATENT ASSIGNEE(S):

EMORY UNIVERSITY

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER                    KIND            DATE

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WO 2001029235                A2 20010426

DESIGNATED STATES

W:

AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC  
NL PT SE

APPLICATION INFO.:

WO 2000-US28747                A 20001018

PRIORITY INFO.:

US 1999-60/159,975                19991018

L8 ANSWER 3 OF 4

PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER:

2000071135 PCTFULL ED 20020515

TITLE (ENGLISH):

ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS

TITLE (FRENCH):

AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE  
BOROPROLINE

INVENTOR(S):

WALLNER, Barbara, P.;

MILLER, Glenn

PATENT ASSIGNEE(S):

POINT THERAPEUTICS, INC.

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER                    KIND            DATE

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WO 2000071135                A1 20001130

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ  
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN  
MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ  
TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK  
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM  
GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2000-US14505                A 20000525

PRIORITY INFO.:

US 1999-60/135,861                19990525

L8 ANSWER 4 OF 4

PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER:

1999004817 PCTFULL ED 20020515

TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT  
 TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOThERAPIE  
 INVENTOR(S): WINKELMAN, James, W.;  
 BRIDGES, Kenneth, R.  
 PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9904817	A1	19990204
DESIGNATED STATES			
W:	AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC		
	NL PT SE		
APPLICATION INFO.:	WO 1998-US15052	A	19980722
PRIORITY INFO.:	US 1997-60/053,696		19970725
	US 1997-60/054,148		19970725

=> d kwic 4

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)

lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;  
 ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and  
 mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including  
 leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin  
 cancer, including melanoma, Kaposi's sarcoma, basal. . .  
 . . .  
 peptides; insulin-like  
 growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane;  
 I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine; isobengazole;  
 isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F;  
 larnellarin-N triacetate;  
 lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia  
 inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone;  
 leuporelin;. . .

CLMEN. . . and

lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;  
 ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and  
 mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including  
 leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin  
 cancer, including melanoma, Kaposi's sarcoma, basocellular. . .  
 . . .  
 and  
 lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;  
 ovarian cancer, including those arising from epithelial cells, stromal

cells, germ cells and

**mesenchymal** cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin

- 24 -

cancer, including melanoma, Kaposi's. . .

and

lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma; ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and

**mesenchymal** cells; pancreas cancer; prostate cancer'; rectal cancer; sarcomas, including leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin

cancer, including melanoma, Kaposi's sarcoma, basocellular. . .

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

15.65

15.86

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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17

FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s jasplakinolide/cn

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L10

118 L9

=> s jasplakinolide

251 JASPLAKINOLIDE



1 JASPLAKINOLIDES  
L11 252 JASPLAKINOLIDE  
(JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s l11 or l10  
L12 279 L11 OR L10

=> s hepatocarcinoma? or mesenchymal or neuroectodermal  
1409 HEPATOCARCINOMA?  
11238 MESENCHYMAL  
1281 NEUROECTODERMAL  
L13 13848 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l13 and l12  
L14 2 L13 AND L12

=> d ibib 1-2

L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:248055 CAPLUS  
DOCUMENT NUMBER: 142:352644  
TITLE: RhoA/ROCK Signaling Regulates Sox9 Expression and  
Actin Organization during Chondrogenesis  
AUTHOR(S): Woods, Anita; Wang, Guoyan; Beier, Frank  
CORPORATE SOURCE: Canadian Institutes of Health Research Group in  
Skeletal Development and Remodeling, Department of  
Physiology and Pharmacology, University of Western  
Ontario, London, ON, N6A 5C1, Can.  
SOURCE: Journal of Biological Chemistry (2005), 280(12),  
11626-11634  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:816528 CAPLUS  
DOCUMENT NUMBER: 140:12638  
TITLE: Two CD95 tumor classes with different sensitivities to  
antitumor drugs  
AUTHOR(S): Algeciras-Schimmich, Alicia; Pietras, Eric M.;  
Barnhart, Bryan C.; Legembre, Patrick; Vijayan,  
Shrijay; Holbeck, Susan L.; Peter, Marcus E.  
CORPORATE SOURCE: The Ben May Institute for Cancer Research, University  
of Chicago, Chicago, IL, 60637, USA  
SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (2003), 100(20), 11445-11450  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s ewing? (2W) sarcoma  
1659 EWING?  
36667 SARCOMA  
4162 SARCOMAS  
100 SARCOMATA

38298 SARCOMA

(SARCOMA OR SARCOMAS OR SARCOMATA)

L15 1277 EWING? (2W) SARCOMA

=> s l15 and l12

L16 0 L15 AND L12

=> s dolastatin 11/cn

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L18 22 L17

=> s dolastatin 11

390 DOLASTATIN

59 DOLASTATINS

404 DOLASTATIN

(DOLASTATIN OR DOLASTATINS)

916607 11

L19 22 DOLASTATIN 11

(DOLASTATIN(W) 11)

=> s l19 or l18

L20 24 L19 OR L18

=> d his

(FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006

L1 171 S JASPLAKINOLIDE

L2 1574 S EWING? (2W) SARCOMA

L3 36 S L2 AND L1

L4 1 S L3 NOT PY>2001

L5 5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

L6 1 S L5 AND L4

L7 37 S L5 AND L1

L8 4 S L7 NOT PY>2001

FILE 'CAPLUS' ENTERED AT 16:18:34 ON 17 APR 2006

S JASPLAKINOLIDE/CN

FILE 'REGISTRY' ENTERED AT 16:18:43 ON 17 APR 2006

L9 1 S JASPLAKINOLIDE/CN

FILE 'CAPLUS' ENTERED AT 16:18:43 ON 17 APR 2006

L10 118 S L9

L11 252 S JASPLAKINOLIDE

L12 279 S L11 OR L10

L13 13848 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

L14 2 S L13 AND L12

L15 1277 S EWING? (2W) SARCOMA

L16 0 S L15 AND L12

S DOLASTATIN 11/CN

FILE 'REGISTRY' ENTERED AT 16:20:17 ON 17 APR 2006

L17 1 S DOLASTATIN 11/CN

FILE 'CAPLUS' ENTERED AT 16:20:18 ON 17 APR 2006

L18 22 S L17  
L19 22 S DOLASTATIN 11  
L20 24 S L19 OR L18

=> s l20 and l13

L21 1 L20 AND L13

=> d ibib

L21 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:816528 CAPLUS

DOCUMENT NUMBER: 140:12638

TITLE: Two CD95 tumor classes with different sensitivities to antitumor drugs

AUTHOR(S): Algeciras-Schimmich, Alicia; Pietras, Eric M.; Barnhart, Bryan C.; Legembre, Patrick; Vijayan, Shriyay; Holbeck, Susan L.; Peter, Marcus E.

CORPORATE SOURCE: The Ben May Institute for Cancer Research, University of Chicago, Chicago, IL, 60637, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(20), 11445-11450  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic

L21 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

AB . . . half are type II. Most of the type I cell lines fall into a distinct class of tumor cells expressing **mesenchymal**-like genes, whereas the type II cell lines preferentially express epithelium-like markers. This suggests that type I and II tumor cells represent different stages of carcinogenesis that resemble the epithelial-**mesenchymal** transition. We then screened the National Cancer Institute database of >42,000 compds. for reagents with patterns of growth inhibition that. .

ST soluble CD95ligand antitumor **mesenchymal** epithelial tumor actin tubulin disruption; antitumor resistance CD95 signaling gene expression carcinogenesis

IT 362-07-2, 2-Methoxyestradiol 1110-02-7, NSC 112167 2222-07-3, Cucurbitacin I 6040-19-3, Cucurbitacin A 6766-43-4, Cucurbitacin K 33069-62-4D, Taxol, analog 82855-09-2D, Combretastatin, analog 102396-24-7D, Jasplakinolide, analog 108675-64-5 111517-68-1, NSC 606195 141172-06-7 630400-59-8, NSC 666608 630400-60-1, NSC 658831 630400-62-3, NSC 666606

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(two CD95 tumor classes with different sensitivities to antitumor drugs)

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
NEWS	9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist \$500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
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=> file caplus

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SINCE FILE

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ENTRY

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FILE LAST UPDATED: 17 Apr 2006 (20060417/ED)

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<http://www.cas.org/infopolicy.html>

=> s cofilin

777 COFILIN

232 COFILINS

L1

814 COFILIN

(COFILIN OR COFILINS)

=> s inhibit?

L2 1822517 INHIBIT?

=> s l1 (L) l2

L3 221 L1 (L) L2

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)

7077 HEPATOCAR?

15151 MESENCHY?

0 NUROECTODER?

1659 EWING?

L4 23829 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l3 and l4

L5 1 L3 AND L4

=> d ibib

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:977858 CAPLUS  
 DOCUMENT NUMBER: 138:52333  
 TITLE: Pharmaceutical composition for diagnosis, prevention  
 or treatment of a tumorous state, comprising a  
 modulator of the actin polymerization state  
 INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial;  
 Subra, Frederic  
 PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De  
 Cachan; Institut Gustave Roussy-IGR; Centre National  
 de la Recherche Scientifique CNRS  
 SOURCE: PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:			FR 2001-7976	A 20010618
			WO 2002-FR2106	W 20020618

=> s actin  
     49687 ACTIN  
     30340 ACTINS  
 L6      52687 ACTIN  
           (ACTIN OR ACTINS)

=> s stabil?  
 L7      1026058 STABIL?

=> s l6 (l) l7  
 L8      2489 L6 (L) L7

=> d his

(FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006

L1      814 S COFILIN  
 L2      1822517 S INHIBIT?

L3 221 S L1 (L) L2  
 L4 23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)  
 L5 1 S L3 AND L4  
 L6 52687 S ACTIN  
 L7 1026058 S STABIL?  
 L8 2489 S L6 (L) L7

=> s 18 and 14  
 L9 19 L8 AND L4

=> s 19 not py>2002  
 3759065 PY>2002  
 L10 8 L9 NOT PY>2002

=> s 19 not py>2001  
 4742175 PY>2001  
 L11 8 L9 NOT PY>2001

=> d ibib 1-8

L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:88952 CAPLUS  
 DOCUMENT NUMBER: 136:242165  
 TITLE: TGF $\beta$  is required for the formation of  
 capillary-like structures in three-dimensional  
 cocultures of 10T1/2 and endothelial cells  
 AUTHOR(S): Darland, D. C.; D'Amore, P. A.  
 CORPORATE SOURCE: The Schepens Eye Research Institute and the Department  
 of Ophthalmology, Harvard Medical School, Boston, MA,  
 02114, USA  
 SOURCE: Angiogenesis (2001), 4(1), 11-20  
 CODEN: AGIOFT; ISSN: 0969-6970  
 PUBLISHER: Kluwer Academic Publishers  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2001:7412 CAPLUS  
 DOCUMENT NUMBER: 134:264229  
 TITLE: Integrin  $\alpha\beta$ 1 engagement disrupts  
 intercellular adhesion  
 AUTHOR(S): Kawano, Kenji; Kantak, Seema S.; Murai, Mutsuhiko;  
 Yao, Chung-Chen; Kramer, Randall H.  
 CORPORATE SOURCE: Department of Stomatology, University of California at  
 San Francisco, San Francisco, CA, 94143-0512, USA  
 SOURCE: Experimental Cell Research (2001), 262(2), 180-196  
 CODEN: ECREAL; ISSN: 0014-4827  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:336418 CAPLUS  
 DOCUMENT NUMBER: 133:87270  
 TITLE: The tetraspan molecule CD151, a novel constituent of  
 hemidesmosomes, associates with the integrin  
 $\alpha\beta$ 4 and may regulate the spatial  
 organization of hemidesmosomes  
 AUTHOR(S): Sterk, Lotus M. Th.; Geuijen, Cecile A. W.; Oomen,

Lauran C. J. M.; Calafat, Jero; Janssen, Hans;  
Sonnenberg, Arnoud  
CORPORATE SOURCE: Division of Cell Biology, The Netherlands Cancer  
Institute, Amsterdam, 1066 CX, Neth.  
SOURCE: Journal of Cell Biology (2000), 149(4), 969-982  
CODEN: JCLBA3; ISSN: 0021-9525  
PUBLISHER: Rockefeller University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1998:517212 CAPLUS  
DOCUMENT NUMBER: 129:170359  
TITLE: Expression of human bone morphogenic protein 7 in  
primary rabbit periosteal cells. Potential utility in  
gene therapy for osteochondral repair  
AUTHOR(S): Mason, J. M.; Grande, D. A.; Barcia, M.; Grant, R.;  
Pergolizzi, R. G.; Breitbart, A. S.  
CORPORATE SOURCE: Viral Vector Lab., Dep. Res., North Shore Univ.  
Hosp.-New York Univ. Sch. Med., Manhasset, NY, 11030,  
USA  
SOURCE: Gene Therapy (1998), 5(8), 1098-1104  
CODEN: GETHEC; ISSN: 0969-7128  
PUBLISHER: Stockton Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1997:269919 CAPLUS  
DOCUMENT NUMBER: 126:260361  
TITLE: Modulation of LDL receptor mRNA stability by phorbol  
esters in human liver cell culture models  
AUTHOR(S): Wilson, G. M.; Roberts, E. A.; Deeley, R. G.  
CORPORATE SOURCE: Department of Biochemistry and Cancer Research  
Laboratories, Queen's University, Kingston, ON, Can.  
SOURCE: Journal of Lipid Research (1997), 38(3), 437-446  
CODEN: JLPRAW; ISSN: 0022-2275  
PUBLISHER: Lipid Research, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1992:145098 CAPLUS  
DOCUMENT NUMBER: 116:145098  
TITLE: Gene regulatory factors of the sea urchin embryo. I.  
Purification by affinity chromatography and cloning of  
P3A2, a novel DNA-binding protein  
AUTHOR(S): Calzone, Frank J.; Hoeoeg, Christer; Teplov, David B.;  
Cutting, Ann E.; Zeller, Robert W.; Britten, Roy J.;  
Davidson, Eric H.  
CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA,  
91125, USA  
SOURCE: Development (Cambridge, United Kingdom) (1991),  
112(1), 335-50  
CODEN: DEVPED; ISSN: 0950-1991  
DOCUMENT TYPE: Journal  
LANGUAGE: English



L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1987:595544 CAPLUS  
 DOCUMENT NUMBER: 107:195544  
 TITLE: Developmental and tissue-specific regulation of  
 $\beta$ -tubulin gene expression in the embryo of the  
 sea urchin *Strongylocentrotus purpuratus*  
 AUTHOR(S): Harlow, Patricia; Nemer, Martin  
 CORPORATE SOURCE: Inst. Cancer Res., Fox Chase Cancer Cent.,  
 Philadelphia, PA, 19111, USA  
 SOURCE: Genes & Development (1987), 1(2), 147-60  
 CODEN: GEDEEP; ISSN: 0890-9369  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1983:140906 CAPLUS  
 DOCUMENT NUMBER: 98:140906  
 TITLE: A yellow crescent cytoskeletal domain in ascidian eggs  
 and its role in early development  
 AUTHOR(S): Jeffery, William R.; Meier, Stephen  
 CORPORATE SOURCE: Dep. Zool., Univ. Texas, Austin, TX, 78712, USA  
 SOURCE: Developmental Biology (Orlando, FL, United States)  
 (1983), 96(1), 125-43  
 CODEN: DEBIAO; ISSN: 0012-1606  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

=> d kwic 3

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB . . . and certain integrins to form large complexes at the cell  
 surface. CD151 is expressed by a variety of epithelia and  
**mesenchymal** cells. We demonstrate here that in human skin CD151  
 is codistributed with  $\alpha 3\beta 1$  and  $\alpha 6\beta 4$  at the  
 basolateral surface of. . . cell surface in association with patches of  
 laminin-5. Focal adhesions are present at the periphery of these  
 clusters, connected with **actin** filaments, and they contain both  
 CD151 and  $\alpha 3\beta 1$ . Transient transfection studies of PA-JEB cells  
 with  $\beta 4$  revealed that the integrin. . . recruitment into  
 hemidesmosomes is regulated by the integrin  $\alpha 6\beta 4$ . We suggest  
 that CD151 plays a role in the formation and **stability** of  
 hemidesmosomes by providing a framework for the spatial organization of  
 the different hemidesmosomal components.

=> s dolastatin or jasplakinolide  
 390 DOLASTATIN  
 59 DOLASTATINS  
 404 DOLASTATIN  
 (DOLASTATIN OR DOLASTATINS)  
 251 JASPLAKINOLIDE  
 1 JASPLAKINOLIDES  
 252 JASPLAKINOLIDE  
 (JASPLAKINOLIDE OR JASPLAKINOLIDES)  
 L12 652 DOLASTATIN OR JASPLAKINOLIDE

=> d his

(FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006

L1 814 S COFILIN  
 L2 1822517 S INHIBIT?  
 L3 221 S L1 (L) L2  
 L4 23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)  
 L5 1 S L3 AND L4  
 L6 52687 S ACTIN  
 L7 1026058 S STABIL?  
 L8 2489 S L6 (L) L7  
 L9 19 S L8 AND L4  
 L10 8 S L9 NOT PY>2002  
 L11 8 S L9 NOT PY>2001  
 L12 652 S DOLASTATIN OR JASPLAKINOLIDE

=> s l12 and l4

L13 8 L12 AND L4

=> s l13 not py>2001

4742175 PY>2001

L14 0 L13 NOT PY>2001

=> s l13 not py>2002

3759065 PY>2002

L15 0 L13 NOT PY>2002

=> d l13 ibib 1-8

L13 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:13464 CAPLUS

DOCUMENT NUMBER: 144:101073

TITLE: therapeutic uses of kinase inhibitors, and compositions thereof

INVENTOR(S): Caligiuri, Maureen G.; Kley, Nikolai A.; Murthi, Krishna K.

PATENT ASSIGNEE(S): GPC Biotech, Inc., USA

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006002119	A2	20060105	WO 2005-US21843	20050617
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2004-580868P P 20040618

OTHER SOURCE(S): MARPAT 144:101073

L13 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1290072 CAPLUS

DOCUMENT NUMBER: 144:46998

TITLE: The X-ray crystal structure of BRCA1 tandem BRCT

repeat and BACH1 phosphopeptide complex and methods  
and compositions for antitumor drug design

INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac  
A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.;  
Smerdon, Stephen J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 360 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409543 CAPLUS

DOCUMENT NUMBER: 142:457053

TITLE: Human protein IAP (inhibitor of apoptosis protein)  
nucleobase oligomers, including dsRNA, shRNA, and  
siRNA, and their use for enhancing apoptosis in cancer  
therapy

INVENTOR(S): Lacasse, Eric; McManus, Daniel

PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2005148535 A1 20050707 US 2004-975974 20041028

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409357 CAPLUS

DOCUMENT NUMBER: 142:457052

TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent

INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.

PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.

SOURCE: PCT Int. Appl., 285 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005119217	A1	20050602	US 2004-975790	20041028
PRIORITY APPLN. INFO.:			US 2003-516263P	P 20031030
REFERENCE COUNT:	6	THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:283298 CAPLUS

DOCUMENT NUMBER: 142:349042

TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms

INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,			

SN, TD, TG  
PRIORITY APPLN. INFO.: US 2003-504310P P 20030918  
OTHER SOURCE(S): MARPAT 142:349042

L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:248055 CAPLUS  
DOCUMENT NUMBER: 142:352644  
TITLE: RhoA/ROCK Signaling Regulates Sox9 Expression and Actin Organization during Chondrogenesis  
AUTHOR(S): Woods, Anita; Wang, Guoyan; Beier, Frank  
CORPORATE SOURCE: Canadian Institutes of Health Research Group in Skeletal Development and Remodeling, Department of Physiology and Pharmacology, University of Western Ontario, London, ON, N6A 5C1, Can.  
SOURCE: Journal of Biological Chemistry (2005), 280(12), 11626-11634  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:816528 CAPLUS  
DOCUMENT NUMBER: 140:12638  
TITLE: Two CD95 tumor classes with different sensitivities to antitumor drugs  
AUTHOR(S): Algeciras-Schimmich, Alicia; Pietras, Eric M.; Barnhart, Bryan C.; Legembre, Patrick; Vijayan, Shrijay; Holbeck, Susan L.; Peter, Marcus E.  
CORPORATE SOURCE: The Ben May Institute for Cancer Research, University of Chicago, Chicago, IL, 60637, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(20), 11445-11450  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2001:924095 CAPLUS  
DOCUMENT NUMBER: 136:31647  
TITLE: Toxicity typing using **mesenchymal** stem cells  
INVENTOR(S): Snodgrass, H. Ralph  
PATENT ASSIGNEE(S): Vistagen, Inc., USA  
SOURCE: PCT Int. Appl., 67 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096865	A1	20011220	WO 2001-US19048	20010614
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,			

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,  
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2412769 AA 20011220 CA 2001-2412769 20010614  
 US 2002045179 A1 20020418 US 2001-881475 20010614  
 EP 1290443 A1 20030312 EP 2001-946335 20010614  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004503255 T2 20040205 JP 2002-510943 20010614  
 PRIORITY APPLN. INFO.: US 2000-211608P P 20000614  
 WO 2001-US19048 W 20010614  
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file pctfull		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	51.50	51.71
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

FILE 'PCTFULL' ENTERED AT 09:07:34 ON 18 APR 2006  
 COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED: 11 APR 2006 <20060411/UP>  
 MOST RECENT UPDATE WEEK: 200614 <200614/EW>  
 FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.

SEE

<http://www.stn-international.de/stndatabases/details/ipc-reform.html> >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE  
 (last updated April 10, 2006) <<<

=> s dolastatin or jasplakinolide

459 DOLASTATIN  
 70 DOLASTATINS  
 477 DOLASTATIN  
 (DOLASTATIN OR DOLASTATINS)  
 171 JASPLAKINOLIDE  
 1 JASPLAKINOLIDES  
 171 JASPLAKINOLIDE  
 (JASPLAKINOLIDE OR JASPLAKINOLIDES)

L16 643 DOLASTATIN OR JASPLAKINOLIDE

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)

770 HEPATOCAR?  
 5688 MESENCHY?  
 0 NUROECTODER?  
 3185 EWING?  
 L17 8782 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l17 and l16

L18 243 L17 AND L16

=> s 118 not py>2001  
488865 PY>2001  
L19 16 L18 NOT PY>2001

=> s 116/clm  
60 DOLASTATIN/CLM  
7 JASPLAKINOLIDE/CLM  
L20 67 (DOLASTATIN/CLM OR JASPLAKINOLIDE/CLM)

=> s 120 and 119  
L21 0 L20 AND L19

=> s 119 not py>2000  
587352 PY>2000  
L22 8 L19 NOT PY>2000

=> d ibib 1-8

L22 ANSWER 1 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2000071135 PCTFULL ED 20020515  
TITLE (ENGLISH): ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS  
TITLE (FRENCH): AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE  
BOROPROLINE  
INVENTOR(S): WALLNER, Barbara, P.;  
MILLER, Glenn  
PATENT ASSIGNEE(S): POINT THERAPEUTICS, INC.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
-----		
WO 2000071135	A1	20001130

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ  
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN  
MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ  
TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK  
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM  
GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US14505 A 20000525  
PRIORITY INFO.: US 1999-60/135,861 19990525

L22 ANSWER 2 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN  
ACCESSION NUMBER: 2000067802 PCTFULL ED 20020515  
TITLE (ENGLISH): FATTY ACID-N-SUBSTITUTED INDOL-3-GLYOXYL-AMIDE  
COMPOSITIONS AND USES THEREOF  
TITLE (FRENCH): COMPOSITIONS D'ACIDES GRAS -N-SUBSTITUTED  
INDOL-3-GLYOXYL-AMIDE ET LEUR UTILISATION  
INVENTOR(S): BRADLEY, Matthews, O.;  
SWINDELL, Charles, S.;  
ANTHONY, Forrest;  
WEBB, Nigel, L.;  
FISHER, Mark  
PATENT ASSIGNEE(S): PROTARGA, INC.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
-----		
WO 2000067802	A1	20001116

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ  
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN  
MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT  
TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG  
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI  
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN  
GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US12752 A 20000510  
PRIORITY INFO.: US 1999-60/133,292 19990510

L22 ANSWER 3 OF 8

ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH):

INVENTOR(S):

PATENT ASSIGNEE(S):

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

PATENT INFORMATION:

PCTFULL COPYRIGHT 2006 Univentio on STN  
2000064946 PCTFULL ED 20020515  
COMPOSITIONS AND METHODS FOR CANCER TREATMENT BY  
SELECTIVELY INHIBITING VEGF  
COMPOSITIONS ET PROCEDES DE TRAITEMENT DU CANCER PAR  
INHIBITION SELECTIVE DE VEGF  
THORPE, Philip, E.;  
BREKKEN, Rolf, A.  
BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM  
English  
Patent

NUMBER	KIND	DATE
WO 2000064946	A2	20001102

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ  
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN  
MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT  
TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG  
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI  
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN  
GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US11367 A 20000428  
PRIORITY INFO.: US 1999-60/131,432 19990428

L22 ANSWER 4 OF 8

ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH):

INVENTOR(S):

PATENT ASSIGNEE(S):

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

PATENT INFORMATION:

PCTFULL COPYRIGHT 2006 Univentio on STN  
2000050016 PCTFULL ED 20020515  
COMPOSITIONS AND METHODS FOR IMPROVING INTEGRITY OF  
COMPROMISED BODY PASSAGEWAYS AND CAVITIES  
COMPOSITIONS ET METHODES POUR L'AMELIORATION DE  
L'INTEGRITE DE CAVITES ET DE PASSAGES CORPORELS  
AFFAIBLIS  
SIGNORE, Pierre, E.;  
MACHAN, Lindsay, S.  
ANGIOTECH PHARMACEUTICALS, INC.;  
SIGNORE, Pierre, E.;  
MACHAN, Lindsay, S.  
English  
Patent

NUMBER	KIND	DATE
WO 2000050016	A2	20000831

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE  
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE  
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX  
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA  
UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW  
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR



GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW  
 ML MR NE SN TD TG  
 APPLICATION INFO.: WO 2000-CA175 A 20000223  
 PRIORITY INFO.: US 1999-60/121,424 19990223

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 1999062510 PCTFULL ED 20020515  
 TITLE (ENGLISH): COMPOSITIONS COMPRISING ANTI-MICROTUBULE AGENTS FOR  
 TREATING OR PREVENTING INFLAMMATORY DISEASES  
 TITLE (FRENCH): COMPOSITIONS RENFERMANT DES AGENTS ANTI-MICROTUBULES  
 POUR LE TRAITEMENT OU LA PREVENTION DE MALADIES  
 INFLAMMATOIRES  
 INVENTOR(S): HUNTER, William, L.  
 PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;  
 HUNTER, William, L.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9962510	A2	19991209

DESIGNATED STATES  
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK  
 EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ  
 LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO  
 RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA  
 ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU  
 TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL  
 PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-CA464 A 19990601  
 PRIORITY INFO.: US 1998-09/088,546 19980601

L22 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 1999055343 PCTFULL ED 20020515  
 TITLE (ENGLISH): CNRE BINDING FACTORS AND USES THEREOF  
 TITLE (FRENCH): FACTEURS DE LIAISON CNRE ET UTILISATIONS  
 CORRESPONDANTES  
 INVENTOR(S): CHEN, Yuqing, E.;  
 HORIUCHI, Masatsugu;  
 DZAU, Victor, J.;  
 TAMURA, Koichi  
 PATENT ASSIGNEE(S): THE BRIGHAM AND WOMEN'S HOSPITAL, INC.;  
 CHEN, Yuqing, E.;  
 HORIUCHI, Masatsugu;  
 DZAU, Victor, J.;  
 TAMURA, Koichi  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9955343	A1	19991104

DESIGNATED STATES  
 W: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC  
 NL PT SE

APPLICATION INFO.: WO 1999-US8502 A 19990423  
 PRIORITY INFO.: US 1998-60/082,997 19980424

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN  
 ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515  
 TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT  
 TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOOTHERAPIE  
 INVENTOR(S): WINKELMAN, James, W.;

PATENT ASSIGNEE(S): BRIDGES, Kenneth, R.  
LANGUAGE OF PUBL.: BRIGHAM & WOMEN'S HOSPITAL, INC.  
DOCUMENT TYPE: English  
PATENT INFORMATION: Patent

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES

W:

AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC  
NL PT SE

APPLICATION INFO.:

WO 1998-US15052 A 19980722

PRIORITY INFO.:

US 1997-60/053,696 19970725

US 1997-60/054,148 19970725

L22 ANSWER 8 OF 8

ACCESSION NUMBER:

PCTFULL COPYRIGHT 2006 Univentio on STN

TITLE (ENGLISH):

1998035554 PCTFULL ED 20020514

COMBINED TUMOR SUPPRESSOR GENE THERAPY AND CHEMOTHERAPY  
IN THE TREATMENT OF NEOPLASMS

TITLE (FRENCH):

COMBINAISON THERAPIE GENIQUE SUPPRESSIVE DE TUMEURS -  
CHIMIOETHERAPIE UTILISEE DANS LE TRAITEMENT DE  
NEOPLASMES

INVENTOR(S):

NIELSEN, Loretta;  
HOROWITZ, Jo, Ann;  
MANEVAL, Daniel, C.;  
DEMERS, G., William;  
RYBAK, Mary, Ellen;  
RESNICK, Gene

PATENT ASSIGNEE(S):

CANJI, INC.;  
NIELSEN, Loretta;  
HOROWITZ, Jo, Ann;  
MANEVAL, Daniel, C.;  
DEMERS, G., William;  
RYBAK, Mary, Ellen;  
RESNICK, Gene

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9835554	A2	19980820

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC  
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH  
GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT  
BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ  
CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:

WO 1998-US3514 A 19980217

PRIORITY INFO.:

US 1997-8/801,285 19970218

US 1997-8/801,681 19970218

US 1997-8/801,755 19970218

US 1997-8/801,765 19970218

US 1997-60/038,065 19970218

US 1997-60/047,834 19970528

=> d kwic 5, 7

L22 ANSWER 5 OF 8

PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . subtilisin, 1069C85, steganacin, combretastatin, curacin,

estradiol,  
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids,  
including  
vinblastine and vincristine, maytansinoids and ansamitocins, rhizoxin,  
phornopsin A,  
ustiloxins, **dolastatin 10**, **dolastatin 15**,  
halichondrins and halistatins, spongistatins,  
cryptophycins, rhazinilam. betaine. taurine, isethionate, HO-221,  
adociasulfate-2,  
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly  
promoting  
protein (taxol-like protein, TALP),. . .

. . .  
phomopsin A (Hamel, Med. Res. Rev. 16(2): 207-23 ) 1, 1996), ustiloxins  
(Hamel, Med Res. Rev. 16(2): 207-23 ) 1, 1996), **dolastatin I 0**  
(Hamel, Med. Res. Rev.

16(2): 207-23 ) 1, 1996). **dolastatin 15** (Hamel. Med Res. Rev.  
16(2): 207-23 ) 1, 1996),  
halichondrins and halistatins (Hamel, Med. Res. Rev. 16(2): 207-231,  
1996),  
spongistatins (Hamel,. . .

. . .  
subtilisin,  
1069C85, steganacin, combretastatin, curacin, estradiol,  
2-methoxyestradiol, flavanol,  
rotenone, griseofulvin, vinca alkaloids, including vinblastine and  
vincristine,  
maytansinoids and ansamitocins, rhizoxin. phomopsin A. ustiloxins,  
**dolastatin 10**,  
**dolastatin 15**, halichondrins and halistatins, spongistatins.  
cryptophycins, rhazinilam,  
betaine, taurine, isethionate. HO-221, adociasulfate-2, estramustine.  
monoclonal anti-  
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endpoints: (1) inhibition of  
the white blood cell response (macrophages, neutrophils and T cells)  
which initiates the  
inflammatory cascade; (2) inhibition of **mesenchymal** cell  
(fibroblasts, synoviocytes,  
etc.) hyperproliferation that leads to the development of fibrosis and  
loss of organ  
function; (3) inhibition of matrix metalloproteinase. . .

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DETD . . . 91)

lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous  
cell carcinoma;  
ovarian cancer, including those arising from epithelial cells, stromal  
cells, germ cells and  
**mesenchymal** cells; pancreas cancer; prostate cancer; rectal  
cancer; sarcomas, including  
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and  
osteosarcoma; skin  
cancer, including melanoma, Kaposi's sarcoma, basal. . .

peptides; insulin-like  
growth factor-I receptor inhibitor; interferon agonists; interferons;  
interleukins; iobenguane;  
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine;  
isobengazole;  
isohomohalichondrin B; itasetron; **jasplakinolide**; kahalalide F;  
larnellarin-N triacetate;  
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin;  
letrozole; leukemia  
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen +  
progesterone;  
leuprorelin;. . .

CLMEN. . . and  
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- 24 -  
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